FISKE FUND PRIZE DISSERTATION, No. XXXIV.

THE PHYSIOLOGICAL AND PATHOLOGICAL EFFECTS OF THE USE OF TOBACCO.

BY

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TO

DR. HORATIO C. WOOD,

PROFESSOR OF MATERIA MEDICA AND THERAPEUTICS
IN THE
UNIVERSITY OF PENNSYLVANIA,

THIS LITTLE
BROCHURE IS RESPECTFULLY DEDICATED,

AS A TRIBUTE TO HIS EMINENCE
AS AN
ORIGINAL INVESTIGATOR,
AND AS
A FEEBLE ACKNOWLEDGMENT OF THE MANY KINDNESSES
WHICH
HE HAS SHOWN THE WRITER.

THE Trustees of the Fiske Fund, at the annual meeting of the Rhode Island Medical Society, held at Providence, June 11th, 1885, announced that they had awarded a premium of two hundred dollars to an essay on "The Physiological and Pathological Effects of the Use of Tobacco," bearing the motto:

"Quid Nimium Probat, Nihil Probat."

The author was found to be HOBART AMORY HARE, M.D., of Philadelphia, Pa.

OLIVER C. WIGGIN, M.D., Providence,
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THE PHYSIOLOGICAL AND PATHOLOGICAL EFFECTS

OF

THE USE OF TOBACCO.

PART FIRST.

An essay on such a subject as the Committee, or rather Trustees, of the Fiske Prizes have chosen is necessarily a difficult task, for several reasons. In the first place the title does not state whether the essay is to be on a basis of scientific research of an original character, or whether the paper is intended, if successful, to be printed for popular reading. The writer has therefore been somewhat "at sea" as regards the object of the essay, and if he has passed the boundary line in either direction in certain instances he must beg the reader's forbearance. It has been his aim to be as concise as possible in his statements, when such conciseness was consistent with clearness, and he trusts that he has succeeded in so doing. Many may suppose that as tobacco has been for so many years a subject for authorship, both for and against its use, much is known about it, in every way. This is a mistake, because much of the writing on the subject has been done by those who were enemies or friends of the weed, and who often knew little or nothing of the subject with which they were dealing. Very few, with certain notable exceptions, were medical men; by far the greater portion of the writers being curates, etc. As a consequence the bibliographer is at first fairly staggered by the great array of books on the subject which are put before him, but soon finds that one work is but a repetition of its predecessor, containing the same "horrible cases of suffering" which have all resulted from the use of the "noxious"

drug. On the other hand quite a large amount of experimental work has been done in Germany, although very little of it is of late date. Various experiments, generally of minor importance, have been performed by English and American writers, most of this being of much earlier date than that already spoken of.

The experiments of Sir Benjamin Brodie and others of his time[1] are interesting as showing a certain epoch in the history of Experimental Therapeutics, the methods of that eminent man being far behind those of the present generation. On glancing over some old Theses for Graduation, written by members of the Medical Department of the University of Pennsylvania about 1824, the writer came upon one with the following curious "title," "The Use of Tobacco in the Resuscitation of the Apparently Drowned," in which the writer, having apologized most humbly for the apparent cruelty of his methods, proceeded to describe how he and a friend had, with commendable desire for knowledge, held various dogs, of all sizes, shapes and ages, under water until they ceased to struggle, often, indeed, holding them under water for "at least three minutes" after all struggles ceased, and then attempting to resuscitate them by giving strong decoctions of TOBACCO per os and rectum. The experimenter further went on to state that "in no case did the animal revive," which cannot be wondered at, considering that tobacco kills by failure of respiration.[2] It should have been stated that the writer quoted mentioned that it had been said of tobacco, it was an efficient remedy in such cases.[3]

Many of the experiments made by the writer were performed in his private laboratory, while others were performed in the Physiological Laboratory of the University of Pennsylvania. These experiments will be marked by a foot-note acknowledging

[1] See portion of this paper relating to Pathological Effects.

[2] See portion of this paper relating to the Physiological Action of Tobacco and Nicotine.

[3] This idea was so thoroughly believed in at one time that apparatus for using tobacco in such cases was placed at various points on the banks of the Seine.

their source, throughout the paper.[1] So far as the writer knows, no one else has as yet made any thorough examinations of nicotinized blood by means of the spectroscope, and for this part of the paper he claims, therefore, entire originality. The experiments on the nervous system and the pupil were merely intended as additional proof of the results reached by others, as were also those on the circulation.

PART SECOND.

The Tobacco of commerce consists of the dried leaves of Nicotiana Tabacum, an annual plant of the natural Order Solanaceæ, which is indigenous to America, but at present is cultivated in all parts of the world. Its leaves are broad and large. It has a five-parted calyx, a funnel-shaped, five-lobed corolla, and five stamens. The flowers grow in panicles at the top of the stem, and the fruit is a two-celled, many-seeded capsule with five valves. The plants are but rarely shrubby in character, more frequently being herbaceous, and covered everywhere by clammy hairs. Besides the species of tobacco already mentioned, we have several lesser species, which are also cultivated to a much smaller extent than Nicotiana Tabacum. Some of these are indigenous to the East, and others are indigenous to America. Nicotiana Rustica, or Green tobacco, is much smaller than the American species, and is more hardy. For this reason it can often be cultivated in northern regions with great advantage. It is sometimes called English tobacco, because it was the first kind introduced into England for cultivation. This variety is about one or two feet shorter than the American plant, and is a native of the East.

The famous Shiraz tobacco is derived from the Nicotiana Persica, which is much esteemed by many smokers, owing to its

[1] The rules of the Laboratory require that in consideration of the use of the apparatus all work performed therein must be acknowledged.

mildness. Turkish tobacco is milder still, and its leaves are small and yellow, or yellowish-brown in color.

The Nicotiana Repanda of Cuba, and the Nicotiana Multivalvis, Quadrivalvis and Nana of the United States, form the rest of the species.

Indian tobacco, so called, is not one of this race or species at all, but is more commonly known as Lobelia Inflata.

The name Nicotiana is derived from that of Jean Nicot, who first introduced the drug on the Continent of Europe.

The name tobacco is, however, of disputed origin. Many consider it a derivative of Tabacos, the Carribean name for pipe, and think that the Spaniards transferred the name to the plant itself. Others believe that it comes from the name of Tabago, one of the islands in the Carribean group, or from Tabacco, a province of Yucatan. A few believe it to be derived from Tabasco, in the Gulf of Florida. The raw leaf does not possess the narcotic and pungent odor of prepared tobacco. This characteristic odor is developed in some cases by moistening the leaves with salt water, and allowing fermentation to take place. The Nicotine in the raw leaf is not volatile, owing to an excess of acid, and the fermentation just alluded to causes a decomposition of the nitrogenous elements of the plant, whereby ammonia is formed, which by its alkalinity overcomes the excess of acid, and the Nicotine thus becomes liberated. To the ammonia and Nicotine is due, to a great extent, the peculiar odor before mentioned.

Many contradictory statements have been made as to the quantity of Nicotine in the raw and prepared leaf.

In the U. S. Dispensatory, 14th edition, by Wood and Bache, the following words are used:—"The proportion of Nicotine contained in prepared tobacco is asserted to be greater than in the fresh." And further on, again, they say:—"It has even been made a question whether Nicotine exists at all in the fresh-growing leaves." A few lines further on the assertion is again made that Prof. Proctor and Prof. Mayer have both decided that Nicotine does exist in the raw leaf, and that the latter

believes it to be in greater quantity in the raw leaf than in the prepared. Boutron and Henry have analyzed tobacco in both conditions, and have found the proportion of Nicotine to be three or four times greater in the raw leaf than in the manufactured article.

Nicotine is an acrid, volatile, colorless liquid, with a hot, burning taste, and an extremely penetrating odor. Perhaps the chief and most important characteristic of this *alkaloid*, chemically speaking, is its entire lack of oxygen, differing from all other alkaloids in this respect, with the exception of Conine and Sparteine.

On exposure to light, Nicotine becomes golden in color, and if exposed for any time to the air, soon has the consistency of tar. Its specific gravity is 1.027, and its chemical formula is, according to Meymott Tidy, $C_{10}H_{14}N_2$.

Many writers,[1] more or less medical, state very positively that there is another active principle in tobacco, namely Nicotianin. Some of them even go so far as to state the methods which were used in obtaining it, and also describe its characteristics and percentages.

The writer found, however, on speaking to Prof. Wormley, of this city, that he knew of no such principle, at least as far as its real presence was concerned, saying that he had read of it, but that it was probably not an active principle but simply some substance which was not characteristic of this drug more than any other.

Through the kindness of Prof. Wormley the writer was able to find the following reference[2] to the alleged discovery of Hermstadt, viz.: Nicotianin.

Vanquelin[3] analyzed it some time ago—speaking of tobacco—and procured an acrid, volatile principle which he called Nico-

[1] Nat'l Dispensatory, Stillé and Maisch; U. S. Dispensatory, 14th Ed., Wood and Bache; Therap., Mat. Med. and Toxicology, H. C. Wood; The Use and Abuse of Tobacco, Lizars, Edin., 1856; Dunglison's Med. Dict.; Worcester's Dictionary.

[2] Christison, On Poisons, Phila., 1845.

[3] Annales de Chimie, lxxi, 139.

tine. "*This substance, which was afterwards obtained in a purer state as a crystalline body, by Hermstadt, has been more recently ascertained by MM. Posselt and Riemans*[1] *to be nothing other than the essential oil of tobacco, which is solid at ordinary temperatures, and they succeeded in obtaining another principle which they consider the true Nicotina.* Wood and Bache (loc. cit.) state that the essential oil of tobacco is chiefly made up of Nicotine, so it is probable, at least, that what MM. Posselt and Riemans considered "the true Nicotina" was identical with the active principle in the essential oil and therefore identical with the substance obtained by Hermstadt. The description of the so-called Nicotianin, as concerns its odor, etc., as well as its effects, corresponds with the odor of what we know of as Nicotine, and the effects which Hermstadt says it produced on him in doses of one grain, namely giddiness and nausea, show its action to be but a counterpart of that of Nicotine.

Moreover, those who assert most positively that Nicotine and Nicotianin are *two separate* active principles give no account of any analysis proving that they are not one and the same thing; in truth, obtained by different methods and having different appearances but only different in these two unimportant particulars. The different methods detailed by Wood and Bache (*loc. cit.*) for obtaining the two principles are briefly as follows.

Hermstadt distilled water from tobacco and allowed the liquid to stand for several days, when a white crystalline matter arose to the surface which had the odor of tobacco and resembled it in its effects; this substance he called "Nicotianin."

The methods given for obtaining Nicotine, consist chiefly in the distillation of water containing tobacco and the addition of some caustic soda, with sometimes some sulphuric acid in the vessel which received the distillate. It will thus be seen that the methods for obtaining these substances resemble each other very closely indeed.

[1] Hist. Stirp. Helvet. Indig., i, 259.

The writer also found that none of the works on Chemistry which were consulted contained any reference whatever to such a substance as Nicotianin.[1] Some of these works are considered so thorough and authoritative that their not mentioning Nicotianin is almost a proof of its being identical with Nicotine, or of its being not an *active principle.*

As Nicotine is easily obtained in crystalline form, as, for example, from nicotinized blood by the addition of mercuric chloride, any claim that Nicotianin is crystalline and Nicotine amorphous is untenable.

Taking all this array of facts against the small authority for the presence of Nicotianin, we must conclude that this so-called principle does not exist as a separate entity and that it should be withdrawn forthwith from our text-books, as at present the mistake is impressed upon the student as a fact. The question which may be asked by the reader is, how is it possible for such a mistake to be perpetuated in works of as high standard as those which have been quoted.

It is very probable that for a certain time the two things were supposed to be entirely different, and this supposition soon crept into the books which were written at that time. Before many years had elapsed the true state of the case was discovered by those who were particularly interested in such matters, while other writers, copying from old works, without looking into the matter, soon managed to perpetuate to the present day a mistake which writers on chemistry do not take pains to correct, simply because for them this misstatement was *long since* shown to be a misstatement indeed.

The quantity of Nicotine in tobacco varies greatly, as may be seen from the following list, containing the results of analyses of several varieties of the "weed":—

[1] Dragendorf, Pflangen Analyse; Muter's Pharmaceutical Chemistry; Attfield's Chemistry; Bloxam's Chemistry; Hermann, Experimental Toxicology; Fownes' Chemistry; Pinner, Organische Chemie; Schörlemmer, Chemistry of Carb. Compounds; Wormley's Micro-Chemistry of Poisons; Watts' Dictionary of Chemistry; Handbook of Modern Chemistry, Meymott Tidy; Wohler's Organic Chemistry.

That from

The Department of Lot in France	8	per cent.
Kentucky	6–8	"
Virginia	6–9	"
Maryland	2.3	"
Havana	—2	"

It should be remembered that these percentages are from the dried leaf and from tobaccos grown in the regions named, for the plant changes both its appearance and constituents according to the soil and climate in which it is placed. The seed of Havana tobacco planted in Kentucky would, in the course of a few crops, change its proportion of Nicotine from minus 2 per cent. to 6 or 8 per cent.

Recently, M. Le Bon announces, after long research, that he has obtained from tobacco *smoke* (1) a notable quantity of Prussic acid; (2) a new alkaloid of a very agreeable odor,[1] but as poisonous as Nicotine. The fiftieth of a drop is sufficient to produce paralysis and death.[2]

Dr. Zulinsky has lately published, in a Polish medical journal, the results of many experiments with tobacco *smoke* on men and animals,[3] and declares that the poisonous characters of the smoke are not alone due to the Nicotine which it contains. He found that even after all Nicotine is removed from the smoke, it still remains very poisonous in large quantities. The second poison which he found in the smoke he calls "Colidin."[4] This substance was not first discovered by Zulinsky, since, in 1871, MM. H. Vohl and Eulenberg[5] found it in the smoke along with pyridine, picoline, lutidine, parvoline, corodine, rubidine and, probably, viridine. The same investigators also found that oxygen, nitrogen, carbonic acid and marsh gas are found in cigar smoke.

[1] A proof that it cannot be what has been called Nicotianin, since that "alkaloid" (?) was supposed to resemble Nicotine in this respect.

[2] Phila. Med. Times, vol. of '79–'80, p. 623.

[3] See Brit. Med. Journal, Oct. 25th, '84, p. 824.

[4] Probably the same as found by M. Le Bon (*loc. cit.*).

[5] Pharm. Jour., Jan., 1872, p. 567.

These observers also state that there is no Nicotine in tobacco smoke, although the tobacco from which the smoke was taken contained 4 per cent. of the alkaloid. Zeise also made this statement, as early as 1843. Vohl and Eulenberg believe the Nicotine which other analysts have supposed to be present to be nothing more than the Nicotine bases, such as those already named. For the rest of their opinions and methods of procedure, the writer must refer the reader to their original paper. They experimented with a mixture containing these bases, and the results were the same as when Nicotine was administered. Even if they are correct in their supposition that there is no Nicotine in tobacco smoke,[1] it concerns us but little, since the effects produced are the same. Although their experiments were most exhaustive, we can hardly accept their results as positively true, in the face of the results of so many able men,[2] unless future analysis confirms them. Dr. Krause,[3] of Annaberg, besides finding Nicotine, hydrogen sulphide and cyanogen in tobacco smoke, found carbonic oxide and carbonic acid, the former in varying amounts. According to this writer, the quantity of these two constituents of tobacco smoke depends upon the kind of tobacco used and the way of filling the pipe, etc. The manner in which the smoke is drawn also affects these products by influencing combustion.

From twelve experiments made by Dr. Krause, it appears that the quantity of carbonic oxide varied from 5.2 to 13.8 in 100 of smoke, the average being 9.3. "As the consumer of the weed never gives out all the smoke he takes in, a certain amount of carbonic oxide poisoning is inevitable." He further states that the sickness of the "first smoke" is largely due to the inhalation of this poison, as well as the Nicotine.[4]

[1] Taylor's Med. Jurisprudence—Reese—p. 255, also makes the assertion, that tobacco smoke contains no Nicotine.

[2] See Dragendorf—Pflangen Analyse.

[3] The Sanitary Record, Nov. 13, 1875.

[4] Herr Kissling, of Bremen, after many experiments, agrees with all the writers quoted except Vohl and Eulenberg. See Dingler's Polytechnisches Journal.

Dr. Zulinsky (*loc. cit.*) states that some of the lighter-colored tobaccos are more injurious, owing to the chemical bleaching, than the darker brands, and says, what sounds like common sense, that the light-colored tobaccos generally give a hotter smoke, owing to the greater quantity of woody fibre which they contain. He admits that the dark brands of tobacco are readily adulterated, but believes them, when pure, to be the best for such use as smoking or chewing. The amount of Nicotine in tobacco *smoke* varies greatly, according to the distance which it traverses before reaching the smoker. The longer the pipe stem, the less Nicotine passes into the mouth, and, therefore, in the cigarette and cigar more Nicotine is inhaled than when a pipe is used. As Nicotine is volatile, much of it is destroyed by the fire, and the balance is partly caught, either by the pores of the pipe or the fibres of the cigar. As it has already been shown that some of the Nicotine is driven off in the process of manufacture, it will readily be seen that very little of the poison, after all, reaches the smoker.

In the old pipe, so soaked with Nicotine as to be unable to absorb more of the drug, it stands to reason that more Nicotine reaches the smoker, and the moral of this is that the pipe is the safest method of using the weed as long as it is comparatively new, but that the cigar is preferable to an old pipe. Every one knows how powerfully an old pipe smells, and how apt it is to "upset" even an old smoker who picks it up to try it. The custom of the Turks is to pass the smoke first through water and then through a long tube before it enters the mouth, and this is probably the wisest way of using the "weed."

The yellowish tinge of the tobacco smoke when puffed from the mouth is due, in great part, to the condensation of the Nicotine as soon as it loses the heat by which it was partially volatilized in the pipe.

When tobacco smoke in any quantity is drawn through water Nicotine in an impure state will discolor the water and adhere to the sides of the vessel at the water line. Smoke derived from an apparatus of this kind will be always whiter and lacking in

the yellowish hue described above. The "biting of the tongue," which is often so severe in smoking, is brought about by several causes which are nearly all absent in the best brands of tobacco. These are as follows, in order of their importance, (1) Nicotine, (2) Heat, varying in amount with the woody fibre in the tobacco, (3) The irritating effects of carbonic acid. The reaction of tobacco smoke is alkaline, owing to the Nicotine, or as Dr. Richardson[1] states the presence of ammonia. The same author believes that the lassitude and sleepiness produced by prolonged smoking is due to this agent—carbonic acid. Taking it for granted that this statement is correct as far as it goes, we can hardly avoid the thought that these symptoms must also be somewhat the result of the Nicotine which has been inhaled.

While it has been shown that an infinitesimal amount of Nicotine in reality reaches the smoker, yet the fact must not be overlooked that a very minute amount of the alkaloid can cause death; even so small a quantity as one thirty-second of a drop will kill cats and dogs.

PART THIRD.

PHYSIOLOGICAL ACTION.

I. ON THE GENERAL SYSTEM.

Dr. W. A. Hammond, of New York, has probably made more extended and thorough researches as to the effects of smoking on the system than any other experimenter, and the writer therefore quotes from his paper[2] ad libitum.

"My manner of living during the succeeding experiments was as follows: I arose every morning at 6 o'clock and retired to bed at 11. I was thus awake seventeen hours and asleep seven hours. The seventeen waking hours were thus appropriated: ten were assigned to study, of as uniform a character as possible;

[1] For and Against Tobacco. London, 1865, p. 5.

[2] Amer. Jour. of the Med. Sci., Oct., 1856, p. 315.

five to daily duties, recreation, etc., and two to a uniform system of physical exercise. The experiments on tobacco embraced the consideration of its effects under the following conditions:—

"1st. When food was sufficient to maintain the healthy balance of the system.

"2d. When a deficiency of aliment was ingested."

He states that he had not previously been in the habit of using tobacco in any form, but had occasionally smoked a cigar without any perceptible effect arising therefrom other than slight nervous excitement. He never in his life either chewed tobacco or used snuff. The tables following are those of Dr. Hammond, but the writer has, for the convenience of the reader, grouped a few of the constant factors in Dr. Hammond's experiments in such a way as to make comparison more easy and the different points more salient.

It should be constantly kept in mind that Tables Nos. 1 and 2 embrace the time during which the experimenter was well nourished, while Tables Nos. 3 and 4 embrace the time when nutriment was deficient. Also that in Tables Nos. 1 and 3 no tobacco was used; but in Tables Nos. 2 and 4, Dr. Hammond smoked 450 grains of tobacco a day, or 150 grains after each meal, which equals about two cigars.

He allowed five days to elapse between the series of experiments with sufficient nutriment and those of insufficient nutriment, in order that the system might be in its normal condition for the second series. On the sixth day, or the first day of the second series, he cut down his daily amount of bread to twelve ounces and his meat to ten ounces. It will be seen from the tables that Dr. Hammond weighed about 225 pounds, and, therefore, was not what would generally be called a lean man, or one of a nervous or excitable temperament. This is worthy of consideration, as tobacco affects people of the latter class more than those of heavy build, etc.

TABLE No. 1.

					URINE.						
	Weight of Body.	Carbonic Acid Gas Expired.	Aqueous Vapor Expired.	Fæces.	Quantity.	Free Acid.	Urea.	Uric Acid.	Chlorine.	Phosphoric Acid.	Sulphuric Acid.
1st day	225.84	11,845.29	4827.50	8.12	40.54	29.43	643.18	13.10	151.62	57.42	39.52
2d day	225.78	11,582 73	4855.91	8.10	41.66	27.82	662.27	12.78	155.16	54.38	36.18
3d day	225.76	11,628.25	4986.70	8.11	42.13	30.51	650.30	12.64	144.25	52.29	35.27
4th day	225.80	11,439.26	4758.37	8.07	42 76	26.17	665.14	12.82	142.51	56.77	35.40
5th day	225.76	11,586.40	4994.85	8.09	41.35	25.39	667.58	12.80	150.52	50.06	38.22
Average,	225.79	11,616.46	4884.66	8.10	40.69	27.86	657.69	12.83	148.81	56.18	36 92

SUFFICIENT FOOD. NO TOBACCO.

Mean temperature of atmosphere was 80.12° Fahr.
Amount of water consumed was 52 oz.; 13 at each meal, and 13 at bedtime.
Pulse was 85 per minute; health excellent; appetite good.
Food well digested.

TABLE No. 2.

					URINE.						
	Weight of Body.	Carbonic Acid Gas Expired.	Aqueous Vapor Expired.	Fæces.	Quantity.	Free Acid.	Urea.	Uric Acid.	Chlorine.	Phosphoric Acid.	Sulphuric Acid.
1st day	225.89	11,726.58	4658.22	8.10	40.21	30.84	628.41	18.29	135.43	88.60	40 59
2d day	225.87	11,562.97	4473.18	8.11	39.63	32.26	610.93	18.80	118.15	84.10	43.17
3d day	225.86	11,839.65	4485.41	8.09	39 80	35.18	614.11	19.03	127.84	75.33	38.65
4th day	225.90	11,710.80	4627.64	8.06	39.45	31.59	604.50	19.01	117.25	81.15	40.10
5th day	225.85	11,482.51	4681.57	8.10	40.02	34.57	618.68	18.45	130.21	70.49	44.15
Average,	225.86	11,664.50	4585.20	8.09	39.80	32.89	615.32	18.71	125.77	80.01	41.33

SUFFICIENT FOOD AND TOBACCO.

Mean temperature of atmosphere was 78.11° Fahr.
Amount of water consumed was 52 oz.; 13 at each meal, and 13 at bedtime.
Appetite good; *food well digested.*
Perspiration apparently slightly diminished.

TABLE No. 3.

					URINE.						
	Weight of Body.	Carbonic Acid Gas Expired.	Aqueous Vapor Expired.	Fæces.	Quantity.	Free Acid.	Urea.	Uric Acid.	Chlorine.	Phosphoric Acid.	Sulphuric Acid.
1st day	225.58	10,672.86	4537.69	6.02	38.74	22 47	623.50	11.58	128.31	45.78	34.54
2d day	225.20	10,384.61	4483.22	6.06	38.20	24.18	615.11	11.23	131.58	43.29	33.09
3d day	224.79	10,350.92	4394.48	6.04	39.04	25.72	604.25	10.01	125.44	44.64	32.22
4th day	224 33	10,526.45	4456.73	6.03	39.57	26.19	601.19	9.82	130.17	42.18	30.15
5th day	223.97	10,347.81	4375.16	6.05	38.73	24.65	608.46	10.04	132.26	45.25	28.31
Average,	224.77	10,456.53	4449.45	6.04	38.85	24.64	610.50	10.53	129.55	44.23	31.66

INSUFFICIENT FOOD AND NO TOBACCO.

Mean temperature of atmosphere was 80.92° Fahr.
Amount of water consumed was 52 oz.; 13 at each meal, and 13 at bedtime.
Pulse was decreased to 86 per minute.
Appetite good; food well digested.
Perspiration increased, owing to extreme heat of the weather.

TABLE No. 4.

					URINE.						
	Weight of Body.	Carbonic Acid Gas Expired.	Aqueous Vapor Expired.	Fæces.	Quantity.	Free Acid.	Urea.	Uric Acid.	Chlorine.	Phosphoric Acid.	Sulphuric Acid.
1st day	223.88	10,508.37	4382.28	4.50	37.85	26.81	569.70	14.91	118.36	72.86	40.21
2d day	223.65	10,495.13	4417.30	4.48	37.29	25.14	541.41	15.11	111.53	75.71	38.02
3d day	223.55	10,265.80	4293.74	4.49	37.15	28.16	536.12	15.29	115.83	78.60	39.00
4th day	223.56	10,483.69	4150.83	4.53	37.48	28.73	552.10	14.80	112.40	74.22	42.23
5th day	223.54	10,478.36	4223·41	4.62	36.92	29.54	540.61	15.17	114.66	70.91	40.58
Average	223.62	10,458.27	4289.51	4.52	37.34	27.67	547.96	15.05	114.55	74.46	40.01

INSUFFICIENT FOOD AND TOBACCO.

Mean temperature of atmosphere was 74.09° Fahr.
Amount of water consumed was 52 oz.; 13 at each meal, and 13 at bedtime.
Pulse was 90 per minute. Appetite good; food well digested.
Perspiration was decreased, owing to cooler weather or the effect of the tobacco.

In regard to the results of these experiments, he sums up as follows:—

(In Tables 1 and 2.) My weight, under the use of tobacco, increased an average of .07 of a pound, the carbonic acid 88.04 grains, the free acid of the urine 4.93 grains, the uric acid 5.88 grains, the phosphoric acid 23.83 grains, and the sulphuric acid 4.41 grains. On the contrary, the quantity of aqueous vapor decreased 299.46 grains, the fæces .01 of an ounce, the urine 1.87 ounces, the urea 42.37 grains, and the chlorine 23.04 grains.

(In Tables 3 and 4.) It will be seen that the loss of weight, owing to deficient food, was lessened from the first, and entirely overcome on the fourth day, by the use of tobacco. In other words, he lost .37 of a pound a day without tobacco smoking, but only lost .09 of a pound a day when tobacco was used.

The excretion of carbonic acid from the lungs was not perceptibly affected, on the average, by the use of tobacco; the amount of aqueous vapor exhaled was reduced 159.94 grains, the fæces 1.92 ounces, the quantity of urine 1.51 ounces, the urea 62.54 grains, and the chlorine 15 grains. The free acid of the urine was increased 3.03 grains, the uric acid 4.52 grains, the phosphoric acid 30.23 grains, and the sulphuric acid 8.35 grains. The desire for food was not nearly as great when he smoked as when he did not.

The conclusions he draws from these results are as follows:—

That smoking does not affect the secretion of carbonic acid through the lungs, but that it lessens the amount of aqueous vapor given off in respiration, diminishes the fæces, *lessens* the *amount* of *urine* and the quantity of its urea and chlorine, and increases the amount of free acid, uric, phosphoric and sulphuric acids eliminated by the kidneys. That tobacco, when food is sufficient to preserve the weight of the body, increases that weight, and when the food is not sufficient to preserve the weight of the body, tobacco restrains the loss. His experiments prove that smoking does not prevent the consumption of fat, but does retard metamorphosis of the nitrogenous tissues.

The writer has reached different conclusions as to the effect

EFFECT OF SMOKING ON THE ELIMINATION OF URINE.

Day.	Hour.	Amount of Urine Passed.	Amount of Water Ingested.	Temperature of Atmosphere.	Remarks.
		oz. dr.			
	9 A.M.	6 4			
1st.	2.30 P.M.	10 1	Twenty-four (24) oz.	29° Fahr.	No tobacco.
	10.30 P.M.	12 1			
		28 6			
	9 A.M.	2 6			
	4 P.M.	13			
2d.	11 P.M.	10 4	Thirty (30) oz	30° Fahr.	No tobacco.
		26 2			
	9 A.M.	5 1			
	3 P.M.	9 7			
3d.	8 P.M.	10 0	Thirty (30) oz.	27° Fahr.	No tobacco.
		25 0			
	9 A.M.	8			
	2.30 P.M.	12 2			
4th.	9.30 P.M.	7 3	Thirty-four (34) oz.	32° Fahr.	No tobacco.
		27 5			
	9 A.M.	9			
	1 P.M.	13 4			
5th.	11.30 P.M.	11	Thirty-four (34) oz.	31° Fahr.	No tobacco.
		33 4			

Total amount of water *passed* in 5 days, 140 oz. and 7 dr.
Total amount of water ingested in 5 days, 152 oz.
Average temperature of atmosphere, 29⅘° Fahr. scale.
Difference in quantity between water passed and ingested, 11 oz. and 1 dr.

Day.	Hour.	Amount of Urine Passed.	Amount of Water Ingested.	Amount of Tobacco Consumed.	Temperature of Atmosphere.	Remarks.
		oz. dr.				
	9 A.M.	7 4				
1st.	2.30 P.M.	12 1	Twenty-six (26) oz.	100 grs.	30° Fahr.	Tobacco used.
	10.30 P.M.	12 1				
		31 6				
	9 A.M.	4 6				
	4 P.M.	13				
2d.	11 P.M.	10 4	Thirty (30) oz.	100 grs.	28° Fahr.	Tobacco used.
		28 2				
	9 A.M.	5 1				
	2.30 P.M.	9 7				
3d.	9 P.M.	10 0	Thirty-two (32) oz.	100 grs.	24° Fahr.	Tobacco used.
		25 0				
	9 A.M.	8				
	2.30 P.M.	12 2				
4th.	9.30 P.M.	9 3	Thirty-two (32) oz.	100 grs.	20° Fahr.	Tobacco used.
		29 5				
	9 A.M.	9				
	1 P.M.	13 4				
5th.	11.30 P.M.	11	Thirty-two (32) oz.	100 grs.	32° Fahr.	Tobacco used.
		33 4				

Total amount of water passed in 5 days, 147 oz. and 7 drs.
Total amount of water ingested in 5 days, 152 oz.
Average temperature of atmosphere, 27° Fahr. scale.
Difference between water passed and ingested, 4 oz. and 1 dr.

Difference in table No. 1, 11 oz., 1 dr.
" " No. 2, 4 oz., 1 dr.
Increase, when smoking, 7 oz.

which smoking has on the elimination of urine. On the preceding page will be found the tables from which he draws these conclusions. The duration of each experiment was five consecutive days, with an interval of five days between the two series of experiments, in order that the results might be entirely independent of each other. Care was exercised that the amount of water ingested during the two series should be identical, although it will be seen that the *daily* amount varied slightly. This variation has no effect on the results or conclusions, as the statistics are treated in bulk. The tobacco was used in the form of cigarettes, each cigarette being weighed before using, and the stump weighed and its weight subtracted after smoking. The same weight of tobacco (100 grains) was smoked each day, and probably produced as full an effect as a much larger quantity would produce in one accustomed to the use of the drug, since the person who performed these experiments NEVER smokes. No liquid food was taken, and the diet during the two series was in every way alike. The water was taken generally at meal times.

The difference in temperature between the two series is not sufficient to have caused the increased quantity of urine noted. It certainly is a fact that tobacco itself does increase the quantity of urine when taken internally. Claude Bernard[1] asserts, with others, that this is so.

Stillé[2] also believes that tobacco increases diuresis, for he says, "On the whole, it seems probable that tobacco might with advantage take the place of Digitalis in the treatment of many dropsies for which that medicine is now prescribed." He also quotes the results of Fowler in cases of dropsy. To seventy-nine cases of dropsy tobacco was given, with the result of twenty-eight cures and thirty-two relieved. It seems scarcely probable that tobacco when taken internally should increase diuresis and when smoked should decrease the elimination of urine. It is an important fact to bear in mind that during Dr. Hammond's experiments the temperature was high, and therefore his urine

[1] Substances Toxique, p. 410.

[2] Therap. and Mat. Med., p. 384, Vol. II.

was naturally decreased by the loss of fluid in perspiration. The observations of the writer were made in winter, perspiration being, therefore, at a minimum. That Nicotine is eliminated by the kidneys is certain, since it can be recovered from the urine. The fact that the quantity of urine is increased points toward this conclusion.

II. ACTION ON THE NERVOUS SYSTEM.

Krocker has proved conclusively that the convulsions in Nicotine poisoning are not cerebral, as they occurred in frogs whose cerebrums had been extirpated. Vulpian found that cutting off the arterial supply of a limb did not prevent the convulsions.[1]

Krocker confirmed this by dividing the nerve trunk, when the convulsions ceased in that limb. Both the preceding experiments were performed by the writer with a corresponding result; thus proving that the first, or convulsive stage of the poisoning is due to the action of the drug on the cord. What this action is, it is difficult to decide. The first thought which occurs to one is that this primary stage of the poisoning, with its convulsive movements, is due to excitation of the motor tract of the spinal cord.

That drugs of a depresso-motor action can produce convulsions is so well known that it is unnecessary to state it here, and originally it was the custom to consider such phenomena as being the result of a primary stimulation, ere the more powerful and true action of the drug came on. Prof. Fraser, of Edinburgh,[2] and Drs. Ringer and Murrell,[3] have found that in *Atropia* poisoning,[4] convulsions and paralysis are often present at one and the same time, that is to say, the animal whose whole cord is apparently paralyzed by atropia may suddenly be seized by a

[1] Comptes-Rendus de la Soc. de Biol., 1859, page 151, quoted by Wood; Mat. Med. and Toxicology, p. 361.

[2] Trans. of the Royal Soc. of Edinburgh, 1869, xxv, 450.

[3] Med.-Chir. Trans., vol. lix, 1876, p. 389; and Jour. of Anat. and Physiology, 1877, p. 517.

[4] These experiments on atropia are quoted merely for the sake of illustration.

tetanoid convulsion. The explanation of this is, that, in the first stage of atropia poisoning every part of the cord is paralyzed, and as the effects of the drug pass off they release the motor cells of the cord, but leave the hypothetical inhibitory centres still paralyzed. The result is that an ungoverned explosion of nerve force takes place on every impulse which the cord receives from the periphery, the so-called hypothetical reflex inhibitory centres being incapable of restraining the discharge. [Although Setschenow long since demonstrated the existence of a reflex inhibitory centre in the base of the brain, and such eminent physiologists as those already mentioned, together with Ferrier, Bernstein, Hermann and Foster, supposed such centres to exist in the cord, no proof *positive* of their existence has been adduced. In some researches recently made on choreic dogs, in the Physiological Laboratory of the University of Pennsylvania, the writer's attention was called, by the experimenter, to the fact that galvanization of the sciatic nerve after section of the cord produced temporary inhibition of the movements.[1] This inhibition probably was due to stimulation of these very centres, and was only temporary, because the centres became exhausted. It seems, then, that the presence of these cells is sufficiently probable to warrant the writer in dropping the term hypothetical.] As the drug with which this paper deals is most undoubtedly a depresso-motor, it seems to the writer that the convulsions of the primary stage of Nicotine poisoning *must* be due to just this depression of the spinal reflex-inhibitory centres.[2]

It certainly is more logical to believe that a drug is always a depressor of nervous matter, never mind what the outward results may be, than to believe it to be an excito-motor at first and a depresso-motor afterwards.

Although in the experiments on atropia[3] (*loc. cit.*) the paralysis

[1] This result is interesting, as showing that choreic movements are probably spinal in their origin, as well as cerebral, as generally supposed.

[2] For an interesting article on Convulsions due to this cause, see Art. by Reichert, Aug. 13th, 1881, in the Phila. Med. Times.

[3] The experiments quoted can be largely found in Wood's Therapeutics.

came first and the convulsions afterwards, the reversed order of things is perfectly possible and probable with Nicotine. In other words, there is no possible reason why the poison should not in this primary or convulsive stage attack the inhibitory spinal centres, leaving the rest of the cord unscathed for the time being; but as the poison becomes more absorbed, its predominating action—namely, that of depression—asserts itself, and we at last have the true character of the drug before us. The paralysis of the second stage of Nicotine poisoning is due to spinal depression, for the writer found that tying the artery of a limb did not prevent the limb from being equally powerless with the unprotected leg in the second stage. Krocker also performed this experiment with a like result. Galvanization of the cord, the writer found, caused no movements in the limbs in this stage.

In order to discover whether the nerve trunks were paralyzed in the stage under consideration, the writer poisoned a frog by a hypodermic dose of $\frac{1}{32}$ drop of Nicotine. The sciatic nerve at first—that is to say, at the very beginning of the palsy—reacted under the galvanic current, but soon refused to respond even to a current of increased power. This would appear as if the paralysis having first attacked the cord, soon after extended to the nerve trunks themselves. Krocker tied the artery[1] in the leg low down, so as to protect the peripheral endings of the nerves, galvanized the nerve above the ligature, and found, by comparing the results with those obtained by galvanization of unprotected nerves, that the peripheral nerve endings were paralyzed before the nerve trunks. In an experiment, the counterpart of that performed by Krocker, it seemed to the writer as if the nerve trunks and peripheral endings were paralyzed simultaneously. During the stage of excitement, there is always present fibrillary muscular contraction, which never, at any time, amounts to a convulsion in itself. The writer repeated an experiment of Krocker's and reached the same results. Tying a tight ligature around the leg of a frog and injecting Nicotine

[1] Therap., Mat. Med. and Tox., H. C. Wood, p. 362.

into the leg below the ligature, nothing more violent than the ordinary fibrillary muscular contraction was noticed; this proves conclusively that the convulsions are not due to peripheral excitation.

The writer also tied the artery and nerve of the leg and injected Nicotine into the distil part of the limb, with naturally the same result as above stated. On the muscular fibre itself, Nicotine seems to have little or no effect, as the writer found that the muscle, even after death, responds readily to the galvanic current.

Vulpian and Rosenthal both agree in asserting that the sensory nerves are not affected by the drug. Lautenbach, however, proves very conclusively, to his own mind, that sensibility is abolished.[1] He found that an animal poisoned by the administration of one drop of Nicotine lost the sense of touch and also of sensation in general, and walked about the room placing the dorsal aspect of the foot to the floor instead of the plantar surface. He also says, in support of his opinion, that when strong electrical irritation of the sciatic nerve is caused, the pupil does not dilate, "this latter being the most delicate test to determine the absence of sensibility." The symptoms which have been quoted afford ground for the opinion of Lautenbach, although the resting on the dorsum of the foot might be due to other causes, such as muscular weakness, or inco-ordination or palsy of the extensor muscles.

That the galvanization of the sciatic nerve, just mentioned, *proves* the sensory nerves to be paralyzed or impaired, is to be strongly doubted, or even thrown aside, since it has been *positively proved* by other observers that galvanization of the cervical sympathetic with the strongest currents fails to cause dilatation of the pupil,[2] either because of oculo-motor spasm, sympathetic paralysis peripherally, or perhaps both.

[1] Phila. Med. Times, May 26, 1877. René also asserts that sensibility is destroyed and that Setschenow's centre is paralyzed. See Thèse de Nancy, 1878.

[2] See Action on the Pupil.

III. ACTION ON THE PUPIL.

A drop of a solution of Nicotine (1 drachm to the ounce) was dropped into the eye of a rabbit and caused immediate myosis, the other eye remaining with a normal pupil. To another rabbit the writer gave a hypodermic injection of Nicotine and in a very short time *both* pupils were contracted. Krocker and the writer both found that the contraction took place in cut-out eyes. Hirschmann asserts, too, that Nicotine always contracts and never dilates the pupil,[1] but Stillé, on the contrary, asserts that the pupils in the primary stage are uniformly dilated.[2] Taylor's Medical Jurisprudence, by Reese, page 253, asserts this also, but as neither writer mentions his reasons or authority for such a statement, it will be evident to the reader that their assertions are lacking the importance which they otherwise might possess. Hirschmann has found that galvanization of the divided cervical sympathetic fails to cause dilatation of the pupil, when contraction has been brought about by the use of Nicotine[3] dropped into the eye. Krocker has confirmed this. He found, however, that while Nicotine contracts the pupil in any dose, large or small, the sympathetic was only affected when large doses were used. In other words, he found that the sympathetic when stimulated by the galvanic current could overcome a contraction, when such contraction was brought about by a small dose of the drug; but if the contraction was the result of a large dose, he found that stimulation of the sympathetic produced no effect, that is, it was paralyzed.

It seems to the writer that this is almost proof positive that Nicotine produces pupillary contraction by stimulation of the oculo-motor, aided, when the dose has been large, by paralysis of the sympathetic peripherally. The objection may be raised that the sympathetic is not really paralyzed by the Nicotine, but that such a severe spasm is brought about by the drug's action on the oculo-motor that the sympathetic is unable to overcome

[1] Bulletin de Therap., lxv, 561.

[2] Therap., Mat. Med., vol. ii, p. 364.

[3] Reichert's Archiv., 1863, quoted by H. C. Wood.

the said spasm. It seems to the writer that this is hardly possible as Krocker found that galvanization of the sympathetic, when the drug was in large amount, had no effect on the contraction. It is clear that the spasm must be very great when galvanization of a divided cervical sympathetic whose peripheral endings are in good condition produces no effect.

As atropia dilates the pupil by paralysis of the oculo-motor peripheral endings, and probably by stimulating the peripheral endings of the sympathetic,[1] its action is directly antagonistic to that of Nicotine, provided, of course, that the conclusions of the writer are correct.

The writer dropped a single drop of a solution of Nicotine (1 ♁ to the oz.) into the eye of a rabbit, and the pupil immediately contracted. After waiting a few moments, in order that the Nicotine might have its full effect, he next dropped ten drops of an atropia solution (4 grs. to 1 oz.) slowly into the same eye, and in a short time[1] the pupil returned to its normal size and corresponded with the untouched eye. The same experiment was performed on the other eye, except that the order of administration of the two drugs was reversed while the doses remained the same. The usual dilatation of the pupil took place after the atropia,[2] likewise the contraction after the Nicotine; but it was noted that although atropia overcame the contraction in the first experiment, sufficiently to cause the pupil to return to its normal size and no more, the Nicotine in the second experiment overcame the dilatation not only enough to bring the pupil to its former size but also to contract it still further, although not to the same extent as when no atropia was used. There are several ways of accounting for what at first sight appears a curious difference.

It may have been due to some one of the drugs escaping largely from the eye before its effects could take place, or, as the

[1] See Therapeutics, Mat. Med. and Toxicology, by H. C. Wood, page 256, for a very clear account of evidence proving that this assertion is probably correct.

[2] Fifteen or twenty minutes elapsed in each case, as usual, before the atropia began to fully act.

volume of the atropia in the first experiment was greater than that of the Nicotine, the atropia may have washed some of the Nicotine away; whereas, in the second experiment, the Nicotine being dropped into the eye last, its full effect could take place. Nicotine is so acrid and so irritating to the eye that it always produces a certain amount of lachrymation, which would naturally wash part of the drug away. As atropia has a local anæsthetic action on the eye, the dropping of Nicotine does not cause such a large amount of lachrymation when atropia has previously been instilled into the eye, as when Nicotine is dropped into an eye whose usual amount of æsthesia is preserved, and, therefore, in the atropinized eye there was less danger of the Nicotine being washed away, and consequently, perhaps, a greater opportunity for the Nicotine to act. The writer also experimented on frogs in the same manner, and obtained the same results. He found that the drugs acted more evenly, and that the reversal of the order of their administration had no perceptible effect as to their respective actions. Krocker asserts that Nicotine causes contraction of the pupil when the eye has been enucleated, which, if true, proves that the action of the drug is largely peripheral, at any rate. The writer has confirmed the experiments of Krocker, using the cut-out eyes of frogs. In every case quite as much contraction took place in the enucleated eyes as when they were yet connected with the governing centres. The writer, furthermore, performed the experiments with the atropia and Nicotine as antagonists. In these experiments, however, he dropped the eyes into the two solutions of the same strength as before. In summing up the results of these experiments, we find:—

First. That Nicotine causes contraction of the pupil.

Second. That the contraction of the pupil is due to peripheral action on the motor nerves of the eye, or, rather, the nerves governing the movements of the pupil.

Third. That this myosis is caused by the drug stimulating the peripheral endings of the oculo-motor and paralyzing the peripheral endings of the sympathetic, when the drug is in very

large quantity. This is proved by the facts that contraction is due to oculo-motor power, that the contraction takes place in the cut-out eye, and also that galvanization of the divided cervical sympathetic does not dilate the pupil when Nicotine has been administered, the last-mentioned fact proving that the sympathetic is paralyzed. Additional, though not positive, proof of this is the antagonistic effects of atropia to those of Nicotine, as detailed above. Another proof of peripheral action is, that a pupil contracted by an internal dose of Nicotine remains contracted after the eye is cut out.

IV. ACTION ON THE CIRCULATION.

The study of the action of Nicotine on the circulation is not as easy as the study of its action on other portions of the organism.

This is because the drug has totally opposite effects if given in large or small doses. Thus, large doses of Nicotine paralyze the pneumogastric, smaller doses stimulate it, and still smaller doses seem to have but little, if any, effect on it.

When variations in dose bring about such variation in result, and when the drug is so powerful as to affect the circulation in such small doses as the sixty-fourth of a drop, it will readily be seen that very contradictory results will often be present, caused by some slight mistake in the amount of the drug administered.

Proceeding at once to our subject proper, let us trace the drug's action in this part of the body, beginning with its action on cold-blooded animals.

If a frog's heart be exposed *in situ* by laying open the thoracic cavity, and a small drop ($\frac{1}{32}$) of Nicotine be placed in the pericardial sac, the heart will first pause in diastole, then begin to beat slowly, and in a few moments begin to increase its pulsations, and also, apparently, the force of its contractions. This is again followed by a fall of rate and force. The writer excised four frogs' hearts, and placed them in strong solutions of Nicotine. Their movements were increased in rapidity and force.

Dr. W. T. Benham[1] found that the pure drug painted over the heart of a rabbit, after the organ had been excised, did not stop its movements but increased them. He also injected the poison into the heart cavities without arresting the movements. It is evidently a fact, then, that Nicotine does not affect the heart muscle. Traube[2] injected Nicotine into the jugular vein of a curarized animal, maintained artificial respiration, and found that the pulse and arterial pressure sink at once to half their original position, but in about twenty seconds rise rapidly, the arterial pressure increasing to two and a half times its normal grade. The pulse rate also is much quicker. This increased action lasts for about a minute, when the arterial pressure and pulse rate commence to fall and they soon drop far below their normal position.

The experiments of the writer were performed on *non-curarized* dogs,[3] and the results are exactly the same as those of Traube's.[4] The only advantage that the writer could discover, in using curare, was the avoidance of the *excessive* increase of pulse force, which on one or two occasions ruined his experiments by driving the pen, in one grand upward sweep, far above the drum, driving the mercury and soda solution right out of the tube and filling it with blood. It was for this reason that he gave the two largest dogs but the $\frac{1}{64}$ of a drop, thereby avoiding the excessive pressure. This rise was probably due to asphyxia as well as cardiac stimulation, since when $\frac{1}{32}$ of a drop was given to the *curarized animal* the rise was not so sudden or so great. To tabulate the results we find:—

1st. That when Nicotine is injected into the jugular vein there is a decrease of arterial pressure and rate.

2d. That this is followed very shortly by an increase of pulse rate and pressure, which soon drives the pen above the drum.

[1] West Riding Lunatic Asylum Reports, vol. iv, 1874.

[2] Allgem. Med. Central-Zeitung, 1862, quoted by H. C. Wood.

[3] See Tables showing results of these experiments on following pages.

[4] See end of paper for some typical tracings of Nicotine's action on the circulation.

3d. That this stage of stimulation is followed in a few minutes by another stage of depression of rate and pressure.

4th. That according to both series of experiments there is, after some minutes (about twenty), an increase of pulse rate considerably beyond the normal number, and according to the experiments of the writer, a decrease of arterial pressure.

The lowering of pulse rate must be due to one, or perhaps two, of several causes. Either the drug depresses the heart's motor apparatus directly or stimulates the cardio-inhibitory

TABLE SHOWING PULSE RATE AND PRESSURE.[1]

The arterial pressure is expressed in millimeters.

Time.	Drug.	Pulse.	Arterial Pressure.	DOG No. 1. Non-curarized.
4.20				Weight of dog about 18 pounds.
4.20 10		114	110–112	
4.20.11	$\frac{1}{32}$ drop.			Injected into the Jugular vein.
4.20.21		30	108– 45	Lowering of pulse rate and arterial pressure in the first
4.20.31		60	40– 59	stage.
4.20.41		60	58– 62	
4.20.51		72	63– 91	
4.21.01		108	95–114	Increase of pulse force and rate in the second stage.
4.21.11		78	116–121	
4.21.21		102	115–141	At this point pen was driven above drum.
4.41.21		144	43– 56	Twenty minutes later shows tracing of fourth stage, or
4.41.31		144	42– 50	increase of pulse rate.
4.41.41		144	45– 50	
4.41.51		138	42– 55	

All these tracings were taken by means of the mercurial kymographion of Fick.

TABLE SHOWING PULSE RATE AND PRESSURE.

Time.	Drug.	Pulse.	Arterial Pressure.	DOG No. 2. Non-curarized.
4.40				Weight of dog about 21 pounds.
4.40.10		108	75– 80	
4.40.11	$\frac{1}{32}$ drop.			Injected into Jugular vein.
4.40.21		90	70– 27	Showing lowering of pressure and increasing diminution
4.40.31		60[2]	69–130	of rate. At this point, viz: 4.40.31, the pen was driven above the drum.
4.43.31		90	111–115	Three minutes later pen was returned to drum, and traced
4.43.41		108	115–110	the third stage, viz: slight fall of pressure and rate.
4.43.51		114	108–105	
4.44.01		106	103–107	
4.44.11		102	101–104	
4.44.21		97	98–101	
4.44.31		98	102–105	
4.44.41		95	101–103	

[1] Experiments performed in the Physiological Laboratory of the University of Pennsylvania.

[2] The rise in the pressure was so sudden that there was not time for any increase of rate ordinarily seen in the second stage.

These two tables show only the first and second stages.

TABLE SHOWING PULSE RATE AND PRESSURE.[1]

The arterial pressure is expressed in millimeters.

Time.	Drug.	Pulse.	Arterial Pressure.	DOG No. 3. Non-curarized.
5.				Weight of dog about 30 pounds.
5.10		168	93– 98	
5 10.01	$\frac{1}{64}$ drop.			Injected into Jugular vein.
5.10.11		72	87–102	Decrease in rate showing first stage. Arterial pressure not
5.10.21		78	101–117	being much affected in first stage, but increasing in
5.10.31		118	117–115	second stage, along with the rate.
5.10.41		124	115–117	
5.10.51		150	116–118	
5.11.01		138	119–122	
5.11.11		150	116–118	
5.11.21		138	120–122	

TABLE SHOWING PULSE RATE AND PRESSURE.

Time.	Drug.	Pulse.	Arterial Pressure.	DOG No. 4. Non-curarized.
2.15				Weight of dog about 25 pounds.
2.15.10		162	85– 88	
2.15.11	$\frac{1}{60}$ drop.			Injected into the Jugular vein.
2.15.21		142	80– 91	Slight fall of pressure showing first stage, followed by the
2.15.31		124	86– 92	fall in rate.
2.15.41		110	88– 94	
2.15.51		142	90– 98	Increase of pressure and rate, showing second stage.
2.16.01		120	95–105	
2.16.11		118	106–108	
2.16.21		142	102–110	
2.16.31		148	104–113	
2.16.41		148	108–115	
2.16.51		120	110–117	
2.17.01		123	113–120	

[1] Experiments performed in the Physiological Laboratory of the University of Pennsylvania.

centres in the medulla or the peripheral endings of the vagi or the ganglion of Ludwig. That the drug does not act on the heart muscle, etc., is proved by the experiments of Dr. Benham (loc. cit.) and the writer. Traube and Rosenthal both state that previous division of the par vagum does not prevent the slowing of the pulse rate after the administration of the Nicotine. This, of course, proves that the action is not centric, at least entirely so.

In the experiments of Tugenhold reported by Rosenthal and quoted by Wood, the primary lowering of the pulse rate amounted almost to diastolic arrest which was not prevented by previous division of the par vagum, but did not occur when very large

doses of woorara were given. As woorara in large doses produces paralysis of the peripheral inhibitory apparatus, Rosenthal argues that the primary lowering of the pulse rate, ending in cardiac diastole often, is caused by stimulation of the peripheral endings of the pneumogastric. The effects of the drug, as already detailed, when applied directly to the heart also tend to prove, with the evidence already brought forward by others, that the action of the drug is at least largely peripheral.[1]

The question as to whether the drug affects the ganglion of Ludwig as well as the peripheral endings of the pneumogastric, is one not easily decided. The only way to decide would be by the use of antagonistic drugs, which is always an uncertain method of research. Other observers[2] have decided that large doses of Nicotine (about $\frac{1}{4}$–1 drop) produce paralysis of the peripheral inhibitory apparatus, without involvement of the centre of Ludwig. It may be considered probable at least that if large doses do not affect Ludwig's ganglion small doses do not either, and we can be pretty safe in believing, therefore, that the ganglion of Ludwig is not stimulated in the primary stage of Nicotine's action.

The increase of pulse rate in the second stage is probably due to PARTIAL paralysis of the pneumogastric peripherally. The reason the action is spoken of as *peripheral* is this: As the inhibitory centre in the medulla is not affected in the first stage, the supposition is at least permissible that it remains intact in the second stage. Traube also found that if the par vagum be cut during this stage, the pulse rate increased still more, which proves, first, that the centre in the medulla was still acting, and second, that the nerve itself was not completely paralyzed, or it could not have transmitted the centric impulse.

The slowing of pulse rate which occurs with the fall of

[1] If atropia, which paralyzes the peripheral inhibitory apparatus, be given in this stage the pulse is immediately increased in rate.

[2] For several interesting studies as to the antagonism etc., of Atropia, Muscarin and Nicotine, see Schmiedeberg-Bericht der Säche; Academie d. Wissenschaften. Mail. Phys. Cl., 1870, 129; also Ludwig's Arbeiten, v, 41.

pressure in the *third* stage is very slight, and is probably due to temporary cardiac exhaustion after the violent efforts of the second stage. Rosenthal also found that stimulation of the pneumogastrics with the strongest galvanic currents produced no effect on the cardiac pulsations in the third and fourth stages.

From this it would appear that the paralysis of the pneumogastrics is one of a creeping character, which in the second stage is merely beginning, but which in the third and fourth stages is complete. In other words, Nicotine acts on the pneumogastric just as other paralyzants of the pneumogastric do, first stimulating the nerve and then paralyzing it. The rise and fall of the arterial pressure is probably largely due to the action, either directly or indirectly, of the drug on the *vaso-motor* system.

The writer found that the rise of pressure was not nearly so great after the injection of $\frac{1}{32}$ drop of Nicotine in the curarized dog as in the non-curarized animal. As Nicotine produces death by asphyxia,[1] it will be readily seen why the arterial pressure would be much greater in the non-curarized than in the curarized animal, in whom artificial respiration was kept up.

We may, therefore, consider that the *rise* is partly due to stimulation of the vaso-motor centre by the asphyxia produced.

The writer also found that the mesenteric capillaries of the frog contracted in the second stage, but became dilated in the third and fourth stages.

That the vaso-motor system is really paralyzed in the later stages, the writer proved by producing asphyxia, which caused no change in the arterial pressure of the dog operated upon.

This does not, however, prove that the centre of the vaso-motor system in the medulla is paralyzed, since the vaso-motor nerves may be so influenced as to be unable to transmit the centric impulse.

The question as to what *part* of the vaso-motor system is affected in the later stages is, therefore, undecided, but that paralysis of some part of the system is present is certainly a fact,

[1] See Action on Respiration.

and the fall of arterial pressure is evidently caused by the vaso-motor disturbance. The fall of pressure in the primary stage is, of course, due to inhibition of the heart.

Below will be found tables showing the effect of smoking on the pulse rate.

Table No. 1 was taken from a person who never smokes.[1]

Table No. 2 from a person who is an inveterate smoker.

TABLE NO. 1.*

Day.		Before Breakfast.	Before Dinner.	Before Supper.
1st.	Normal	65	66	66
	Abnormal	98	80	90
2d.	Normal	60	68	67
	Abnormal	97	83	92
3d.	Normal	63	64	63
	Abnormal	95	89	88
4th.	Normal	67	66	66
	Abnormal	98	87	98
5th.	Normal	66	65	64
	Abnormal	94	82	94
Normal average		64	66	65
Abnormal average		96	84	92

Day.		After Breakfast.	After Dinner.	After Supper.
1st.	Normal	67	66	66
	Abnormal	85	72	78
2d.	Normal	66	67	68
	Abnormal	87	74	76
3d.	Normal	62	64	66
	Abnormal	84	71	74
4th.	Normal	64	67	64
	Abnormal	86	82	76
5th.	Normal	66	65	64
	Abnormal	84	81	72
Normal average		65	70	66
Abnormal average		85	76	73

TABLE NO. 2.†

Before Breakfast.	Before Dinner.	Before Supper.
54	66	63
72	78	72
54	60	66
72	78	60
63	72	63
81	78	72
57	72	72
72	81	72
57	72	72
72	78	81
57	68	67
74	79	73

After Breakfast.	After Dinner.	After Supper.
69	57	69
72	75	69
78	90	63
78	96	72
72	81	63
78	87	72
66	75	66
78	84	69
66	69	69
81	81	78
60	74	66
77	85	72

* In all cases, although the pulse rate was increased, the arterial pressure or tension was diminished markedly. Person is *not accustomed* to the *effects of tobacco*. These changes were caused by smoking, rapidly, one cigarette.

† In all cases, although the pulse rate was increased, the arterial pressure or tension was diminished markedly. Person is an *inveterate* smoker. These changes were caused by rapidly smoking one cigarette. This person never uses tobacco otherwise than by smoking.

It will be seen in the preceding tables that smoking invariably caused increase of pulse rate, although the time of day and the presence of food in the stomach governed the degrees of increase

[1] See end of paper, showing tracings of pulse before and after smoking, as taken by the use of Marey's sphygmograph.

very strongly. It will also be noted that the increase of pulse rate was greater in the person unaccustomed to the drug than in the person who was a constant smoker, a result which one would expect.

In Table No. 1 there was a greater increase before breakfast than at any other time of day, and in both tables the increase was greater in the morning than at noon or night, although in Table No. 2 the increase after breakfast was as great as before, although the normal pulse after breakfast was higher than before that meal. It is a rather curious thing that all through Table No. 2 the increase of rate after smoking was the same after meals as before, notwithstanding the fact that the meals always increased the normal rate.

V. ACTION OF THE DRUG ON THE RESPIRATION.

When $\frac{1}{32}$ drop of Nicotine is injected into the jugular vein of an animal, the respirations almost instantly become rapid and very deep, the chest walls being expanded to their greatest extent, and both inspiration and expiration are accompanied by a peculiar whistling or hissing sound, which is probably due to spasmodic contraction of the larynx, as it does not occur when the animal breathes through a tube in the trachea.

The conjunctiva and the membranes of the mouth are intensely congested and dark. There is a very forcible up and down movement of the whole larynx. This lasts for a few moments only, when the respirations become slower than normal. The ordinary tracings of arterial pressure show, in the non-curarized animal, that asphyxia is present, by the characteristic asphyxia curves. That the drug produces death by depressing the respiration, has been proved by Bernard, Van Praag, Kölliker and Albers, and that this depression is due to centric action on the part of the drug is proved by the fact that the breathing is not changed by section of the vagi.

All observers, with one exception, namely, Brodie, assert most positively that the heart continues to beat for some time after the respirations have ceased.[1]

[1] Phila. Med. Times, May 12, 1877; art. by F. L. Haynes.

In twenty dogs which were killed by Nicotine, in the course of the writer's experiments, death occurred invariably from stoppage of respiration; in every case the heart pulsated some moments after respirations ceased.

VI. ACTION ON THE BLOOD.

EXAMINATION—MACROSCOPIC AND MICROSCOPIC.

The action of Nicotine on the part of the organism considered under this heading is twofold; both effects, however, depending on entirely different modes of action. If a small amount of Nicotine be injected into the jugular vein of an animal, the blood on the arterial side of the circulation, in the course of a few minutes (about five) becomes equally dark in appearance with that on the venous side, and if the jugular be opened on one side of the neck and the carotid be opened on the other side, the observer will be unable to tell which is venous and which is arterial blood, except by the interrupted flow of the latter. That this dark hue of the arterial blood is largely dependent on the asphyxiating powers of the drug is proved by the fact that if shaken up with air the blood regains, to a certain extent, its normal arterial hue.

The effects of the drug on the corpuscular elements of the blood are quite interesting. The writer found that the red corpuscles were always crenated, and if the amount of the poison was very large, partial disintegration appeared to take place.

The corpuscles, instead of arranging themselves in rouleaux, formed themselves in rows, as ducks walk one behind the other, the edge of each corpuscle touching the edge of its predecessor. When the poison was added on the stage of the microscope the red corpuscles seemed to shrink and decrease their diameter, losing to a great extent their bi-concave shape and shortly becoming colorless and transparent. Occasionally a corpuscle would seem to be spiculated, resembling somewhat a horse-chestnut, but with fewer spicules.

On the *white* or *colorless* corpuscle the action of the poison is

marked. When this corpuscle is moving on the warm stage the addition of Nicotine instantaneously arrests its movements and breaks it up into eight or more divisions or segments, which now and then become detached and float off by themselves. These divisions are round and resemble the red corpuscle considerably in shape.

The globular form which is often assumed by the white corpuscle does not appear after the addition of Nicotine. On the contrary the movements stop, leaving the protoplasmic process in the position last taken and unretracted.

EXAMINATION—SPECTROSCOPIC.

The usefulness of the spectroscope in physiological, as well as other examinations, is so universally conceded that a paper of this character would not be complete without some spectroscopic examination of the blood under the various conditions which are brought about by Nicotine. Before detailing the experiments, etc., which the writer performed with the aid of the spectroscope on nicotinized blood, it may be well to recall to the reader, very briefly, the methods by which such examinations are made.

Any one using the spectroscope as a tyro, will find that the mere examination of normal hæmoglobin will not impress the true spectra sufficiently strongly on his mind to enable him to distinguish changes which may take place in the poisoned or altered solution; and it is therefore advisable for the beginner to have two glass cells, one centimetre in diameter, in one of which, the lower preferably, can be placed the normal standard solution, the upper cell being reserved for the fluid which it is desired to analyze. The bottoms of the cells should be made of thin "cover glass," such as is used in microscopic work, in order that the two spectra may not be too widely divided.

The capacity of the two cells should be equal, and the glass of which they are made should be of the same thickness.

The lower cell should be full enough of the liquid to allow the under surface of the upper cell to come in contact with the

solution. The reader will pardon the writer if he adds a few notes which may refresh the memory in regard to hæmoglobin and its changes of spectra, etc.

It should be remembered that blood removed from an animal while living shows the spectrum of oxyhæmoglobin, provided that the animal is not influenced by some agent or drug which normally is not present in his system, and that the blood be examined soon after death; because blood outside the body becomes reduced in a few hours, even when in a tightly stoppered bottle.

Venous blood contains enough oxygen to give the spectrum of oxyhæmoglobin, and the spectroscope will not show any difference between arterial and venous blood while life is present. This is not so after death, since Dr. MacMunn has proved that venous blood after death gives the spectrum of reduced hæmoglobin.[1] The same observer also found that the reduction took place in the act of dying, and was not the result of decomposition.[2] If death is caused by asphyxia, however, the arterial and venous blood immediately after death gives the spectrum of reduced hæmoglobin, because the tissues in such cases abstract the oxygen from the blood and the blood also consumes its own oxygen.

It should be borne in mind that oxyhæmoglobin and oxidized hæmoglobin are one and the same thing, and that reduced hæmoglobin, hæmoglobin and deoxidized hæmoglobin are also synonymous.

When a strong solution of oxyhæmoglobin or of freshly-drawn arterial or venous blood is placed before the slit in the spectroscope, all light is cut off; as more water is added, the characteristic spectrum of oxyhæmoglobin appears between the orange-yellow and the green, and, therefore, nearest the redward side of the field. If still more water be added, this solid band divides into two bands, of which the one next the orange-yellow is the

[1] The Spectroscope in Medicine, MacMunn, p. 71.

[2] This reduction is not seen after death from cold or starvation, owing to diminished reducing power of the tissues.

most pronounced, while the band next the green is wider, but more washed out.

On diluting still more, we narrow these bands, and finally only the redward band is left, which, on another addition of water, also disappears.

Preyer has found that a solution of oxyhæmoglobin, of the strength of 0.08 per cent., always gives the full absorption band. The writer has found that blood requires a dilution of fifteen times to give the same spectrum.

The spectrum of oxyhæmoglobin is darkest, or as dark at the edges of the band as at its centre, while that of reduced hæmoglobin is darkest in the centre and shades off lightly at the edges. In the reduced solution, the spectrum has its centre where the unreduced spectrum would, if diluted, divide. It also "blocks out" more of the orange-yellow than does the oxyhæmoglobin band, and does not dim the blue side of the spectrum as much as the unreduced solution; as a consequence, the latter lets through the red and orange-yellow rays, and the former the red and bluish rays.

EXPERIMENT NO. I.

In the Lower Cell.—A solution of normal[1] (?), defibrinated blood of sufficient strength to show the absorption band of hæmoglobin.

In the Upper Cell.—The same solution, to which was added one drop of Nicotine.

The changes resulting were not marked enough to be at all conclusive. The orange-yellow was slightly increased in width, and the hæmoglobin band narrowed correspondingly on that side; the width of the absorption band being decreased by the encroachment of the orange-yellow.

[1] This defibrinated blood had been dried and kept in the Physiological Laboratory for some time. The writer could not discover whether it had been obtained from a normal source or not. The results, such as they are, are, therefore, open to the accusation of being fallacious. It is hardly necessary to add that the spectrum was that of REDUCED hæmoglobin.

There was a dim lightening in the centre of the band, which suggested the separation of the solid band into the two bands which are seen when a strong solution of oxyhæmoglobin is diluted.

EXPERIMENT NO. II.

In the Lower Cell.—A dilution of blood, obtained immediately after death, which was caused by Chloral, not for any purpose on the part of the writer, but in the course of an experiment performed by some one else. As this blood was obtained after death the spectrum was that of reduced hæmoglobin.

In the Upper Cell.—The same solution, to which was added two drops of Nicotine. The following changes took place. The orange-yellow, which was slightly increased in its dimensions in the first experiment, was still more increased in the one before us. The absorption band was correspondingly narrowed on the redward side as the width of the orange-yellow increased.

EXPERIMENT NO. III.

In the Lower Cell.—A dilution of arterial blood taken from a young and healthy dog before any of the Nicotine had been administered.

In the Upper Cell.—A dilution of arterial blood taken from the same animal after the venous injection of one-half drop of Nicotine.[1] As usual in Nicotine poisoning the blood was darker than normal. The change was very marked. The band was divided into two bands in a manner somewhat resembling the division which takes place when a normal and strong solution of oxyhæmoglobin undergoes further dilution.

This *separation* differed from the almost inappreciable separation which took place in Experiments Nos. 1 and 2. It was very marked and was as wide as the *band* is on the left of the observer in a oxyhæmoglobin solution of about 0.09 per cent. Through this break appeared the light as olive-green. The

[1] The dilution in all these experiments was strong enough to give one broad band, undivided.

absorption band on the left was dim and filmy. The orange-yellow was widened.

EXPERIMENT NO. IV.

In the Lower Cell.—A dilution of normal arterial blood.

In the Upper Cell.—A dilution of blood from the same animal, abstracted from the artery just before death, caused by one-half drop of Nicotine. The heart was still beating but respiration had just stopped and the blood had the characteristic darkened hue such as Nicotine always produces in poisonous doses. In this case the blood was particularly dark.

The result was the same as in Experiment No. 3, only more marked, the absorption band being separated and the band on the left-hand side of the observer being still more filmy than before.

The orange-yellow was correspondingly increased in width with the dissolution of the band just mentioned.

The olive-green seen between the bands was also increased in width and intensity. There was no displacement of the bands either to the right or left side.

EXPERIMENT NO. V.

In the Lower Cell.—A dilution of normal arterial blood.

In the Upper Cell.—In this cell was placed some of the blood of Experiment No. 3, which had been brightened in appearance by shaking with the air. The dark color was almost all gone.

The result was the same as in those cases which were not shaken with air.

This experiment was then performed on the still more darkened blood of Experiment No. 4, with the same result. The object of this shaking with air being to supply the blood with oxygen which it may have lost owing to the asphyxia produced by the poison.

This was probably the cause of its dark hue, in part, at any rate, since, as already stated, the color became more arterial when the blood was shaken with air.

EXPERIMENT NO. VI.

In the Lower Cell.—A dilution of normal arterial blood.

In the Upper Cell.—A dilution of blood drawn from an artery of a dog poisoned by one-fourth drop of Nicotine.

The changes noted were not as marked, owing, perhaps, to the small amount of the dose, as in Experiments Nos. 3 and 4.

The chief point noticed was the increase of the orange-yellow associated by corresponding decrease of the band of absorption, in the same manner as has been described in some of the experiments already detailed. The separation of the bands which was so marked in the other experiments was so slight and indistinct as to cause doubt as to its presence, although the writer could discover in the centre a faint shade of olive-green. Aside from this indistinct and uncertain change the band resembled that of reduced hæmoglobin in the way it shaded off at the edges.

EXPERIMENT NO. VII.

In the Lower Cell.—A dilution of normal arterial blood from a dog.

In the Upper Cell.—A dilution of arterial blood, after the venous injection of one and one-half drops of Nicotine. The characteristic dark hue was present and was well-marked. In order to avoid any errors which might arise, owing to the asphyxia produced by the drug before death, the writer passed a constant stream of oxygen through the dilution, the color being more arterial after this procedure. When examined before the slit in the spectroscope the spectrum was altered in the same manner as before. The redward band was narrowed and the orange-yellow increased and there was a marked widening in the split in the spectrum. The edge of the redward band on the orange-yellow side was not clearly outlined but filmy in appearance.

EXPERIMENT NO. VIII.

In the Lower Cell.—A dilution of the poisoned blood, showing the abnormal spectrum, already described.

In the Upper Cell.—A dilution of the same blood, through

which a stream of oxygen was passed for about fifteen minutes. The two cells were filled with poisoned blood in this experiment, in order that the two abnormal spectra might be the more closely compared. Although the hue of the blood through which the oxygen was passed was more arterial than the other, the spectra were the same.

It will be seen that in every case the orange-yellow was widened, which is somewhat remarkable, since the redward band is normally more constant and pronounced than its fellow.

To sum up the results of these experiments: We find that the most constant change produced by the Nicotine was the encroachment of the orange-yellow rays on the redward side of the absorption band. We also find that where the poison was in fairly large quantity, the band was divided just as a dilute oxyhæmoglobin band would be, although the spectrum, which one would expect, would be that of *reduced* hæmoglobin, owing to the asphyxia and the dark color of the blood. In Experiment No. 6, where the amount of the poison was very small, the change was not as marked as in the other experiments; although the redward portion of the band was decidedly encroached upon, the blood was not profoundly enough affected to show the split in the band. The band, therefore, as before stated, resembled that of reduced hæmoglobin, in the filmy outline of its edges and the lack of division in the band itself. The fact that the blood became more arterial in hue when shaken with air and when oxygen was passed through it, combined with the resemblance of the spectrum in Experiment No. 6 to that of reduced hæmoglobin, would seem to prove that the oxyhæmoglobin became reduced, either by the asphyxia which was present, or by some direct action of the drug on the red corpuscle and its contained oxyhæmoglobin. When we consider that blood, when shaken with air, and through which oxygen had been passed, gave the same identical spectra as before such procedure took place, we must come to the conclusion that Nicotine acts *directly on the oxyhæmoglobin*, and that the probable reduction which takes place is due to this action, combined with

asphyxia. The disintegration of the red blood corpuscles, already noted, points to the correctness of this conclusion.

Death, then, occurs in Nicotine poisoning, not simply from ordinary asphyxia, owing to depression of the respiratory centre in the medulla, but also by the failure of the hæmoglobin to carry oxygen to the various portions of the body.

VII. ON THE CUTANEOUS ABSORPTION OF NICOTINE.

It may be interesting to quote the experiments of Dr. M. A. Randolph and Mr. S. G. Dixon on this part of our subject.[1] These experiments were performed in the laboratories of the University of Pennsylvania. In these experiments they used only rabbits of ascertained good health. "The fur of the abdomen was carefully clipped (not shaved), sufficient time, usually seven days, being allowed to intervene between this operation and the application of the drug to the skin, thus permitting any slight scratch made at this time to fully heal. The absence of cutaneous lesions was further confirmed by closer examination under a strong hand magnifier. The drug was then applied to the skin, no friction being used. In order to preclude the possibility of its vaporization and subsequent absorption by the lung surface, the Nicotine was placed upon an adhesive plaster, the backing of which was made of sheet rubber. The plaster, with the drug in its centre, was then applied, in the open air, on a windy day. Different doses were applied; thus, in one case, one drop of Nicotine applied to the skin caused death in five hours and eleven minutes. In each of three cases a similar application of ten drops was fatal in respectively one hundred and nine minutes, twenty-eight minutes and thirty-six minutes. In the fifth case, a similar application of fifteen drops of Nicotine caused death in twenty-eight minutes."

"Of the ante-mortem symptoms, contraction of the pupil was CONSTANT, and often appeared very quickly. Other prominent symptoms were great trembling, with subsequent loss of mus-

[1] See Proceedings of the Academy of Natural Sciences of Phila., Nov. 11, 1884.

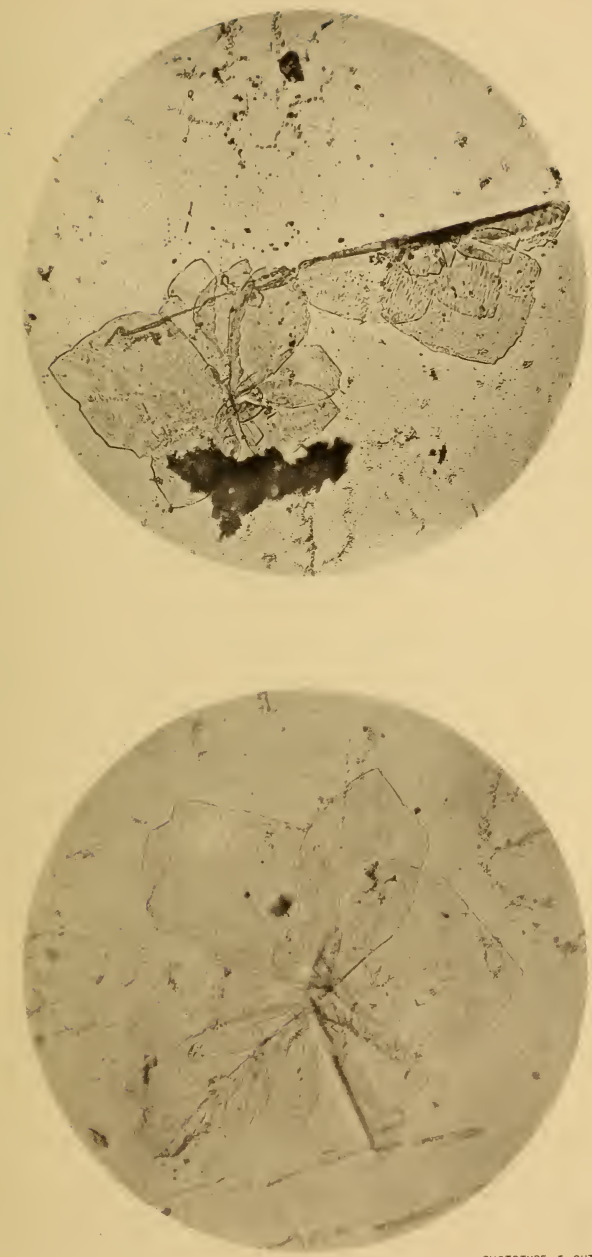
cular power in the extremities. In one case, actual convulsions were noted, and in others, coldness of the skin and increased lachrymal and nasal secretion. Immediately upon the death of two of the animals (after the ten and fifteen-drop doses respectively), blood was removed, defibrinated, and tested with mercuric chloride for the presence of Nicotine, in the manner detailed by Wormley ('Micro-Chemistry of Poisons'). In each of these two instances, characteristic groups of crystals were found upon microscopic examination of the extract from the blood."

Dr. Randolph has been kind enough to send the writer microphotographs of the crystals of Nicotine and mercuric chloride which he found in the blood after death from the cutaneous absorption of Nicotine. (See Plates.)

VIII. ON THE INTESTINES.

Nasse[1] has found that when Nicotine is injected into the jugular vein, a tetanic contraction of the whole intestinal tract takes place, and that section of the vagi or compression of the abdominal aorta did not affect the contraction. The splanchnics were unable to exercise their inhibitory influence, either because they were paralyzed or because the spasm was too intense for them. The writer also saw the tetanic contraction which was always accompanied by defecation. He also compressed the abdominal aorta, and the result was the same as above stated. In his experiments on the pupil the writer found that the sympathetic was paralyzed peripherally, and that there was probably an unconquerable oculo-motor contraction. The results before us correspond exactly with the results that have already been obtained, and reasoning by analogy, which is in this case most direct, we must come to the conclusion that Nicotine paralyzes inhibition everywhere, on the heart, pupil and intestines, and that it stimulates involuntary muscular fibre, as, for example, that of the iris and intestinal canal.

[1] Beiträge zur Phys. der Darmbewegung, Leipsic, 1866, quoted by H. C. Wood.



PHOTOGRAPH, GEO. A. PIERSOL, M.D. PHOTOTYPE, F. GUTEKUNST.

COMPOUND CRYSTALS OF NICOTINE AND MERCURIC CHLORIDE.

Extracted from the Blood of a Rabbit, after Cutaneous Absorption.

IX. ON THE ACTION OF THE LIVER ON THE EFFECTS OF THE DRUG.

Under the head of original communications, in the Phila. Med. Times for May 20th,[1] 1877, Dr. B. F. Lautenbach gives some very interesting accounts of the action of the liver on Nicotine. He determined that one drop of Nicotine would kill a large dog if injected into the general circulation. He then injected one drop of the poison into the mesenteric or splenic vein or into the small intestine, thus forcing the poison to pass through the liver before entering the general circulation. The result being that the animal *recovered* from the effects of the poison in from fifteen minutes to an hour, and appeared like a normal dog. He also found that even two drops of Nicotine fail to kill a dog when the poison first passes through the liver. When the drug is injected into the subcutaneous tissue in a one-drop dose the animal has more intense symptoms and often dies in one minute from the time of injection.

Dr. Lautenbach also found that if the vena porta be tied trismus and tetanus were produced, and death came on rapidly, although the dose was but one-fifth of a drop.[2]

The experimenter also found that one-tenth drop of Nicotine killed frogs, of the esculenta and temporaria species, very rapidly.

One-twentieth drop always produced severe symptoms but never death.

When one-fortieth drop of the poison was given to frogs, whose livers were *extirpated, death occurred,* while in a large number of experiments with the normal frog "no symptoms whatever" were produced by the same dose. The same frogs, four hours later, when given the same amount as before, their livers being in the meantime extirpated, died, with symptoms exactly the same as their predecessors.

[1] On a New Function of the Liver, page 387.

[2] The experimenter found that ligation of the vena porta caused death very shortly. For the symptoms which were produced I must refer the reader to the reference given; the portion here quoted being but a small part of a very interesting paper, which will well repay any one who takes the trouble to look it up.

Hyperæmia of the liver was now ingeniously produced,[1] in order to discover whether activity of that organ affected the size of the *fatal* dose. When one-tenth drop—the fatal dose for a normal frog—was administered "not the slightest symptom was observed," nor would one-fifth drop cause death. Showing most conclusively that greater activity on the part of the liver prevents the poison from acting, even in large doses. In other words, the liver seems to destroy the poison.

Dr. Lautenbach went still further, macerated the livers of dogs and rabbits with from 3–5 drops of Nicotine, and injected the expressed juice into dogs and frogs. The animals showed mild symptoms of Nicotine poisoning, but did not on any occasion die. When the juice was given to three liverless frogs they only showed slight symptoms.

As counter experiments Lautenbach macerated the kidneys and added Nicotine, and the animals treated with this juice all died.

The experimenter then draws a conclusion which is of great practical interest, viz.: There is no danger from the effects of chewing tobacco, because any Nicotine which is swallowed passes through the liver, while the Nicotine inhaled with smoke passes into the general circulation through the lungs.

If this theory held good in practice we should find that the small boy, for example, would be more sick from his first smoke than his first chew, and this is not often the case, possibly because of the constant contact of the drug with the mucous membrane of the mouth, where chewing is practiced. Dr. Lautenbach in this paper just quoted naturally comes to the conclusion that the liver destroys Nicotine. In a later paper,[2] however, he comes to somewhat different conclusions; the reasons for his change of opinion being as follows: In later experiments he found that Nicotine, when injected into a vein of the general

[1] For method of procedure, see Phila. Med. Times.

[2] Phila. Med. Times, vol. x, No. 523. On the Difference in the Effects produced by Nicotine when Injected into an Efferent, from those produced by the introduction of the poison into an Afferent Blood Vessel.

circulation, produced death in the rabbit in a half-drop dose, while if *three-quarters* of a drop was injected into the femoral artery of an animal of the same species there resulted, not death, but only poisonous symptoms, and the animals recovered in less than two hours.

When he injected one-half drop of the poison into the carotids of cats convulsions were produced, but *not death.* These experiments appear to prove that it is only necessary for Nicotine to pass through a series of capillaries to be deprived of its poisonous properties and the liver has no specific effect of its own. The whole line of evidence is so contradictory that it is somewhat difficult to arrive at a correct or satisfactory conclusion.

When the drug was injected into the femoral artery, we can readily understand that its action would be slower and more dispersed than when injected into a vein by which it would be sent directly to the heart and other vital points.

The passage of the poison would be delayed, and, instead of rushing *en masse* on the vulnerable points, would attack them in such small detachments that the animal would survive.

The results of the injection of the poison into the carotids of cats are not to be compared to those obtained by the experimenter with other animals, since cats are notorious for their tenacity of life, while rabbits are quite the contrary.

The fact that the capillaries often rob a poison of its toxic properties is well known among physiologists, and Lautenbach's statements in this respect are by no means new.

PART FOURTH.

PATHOLOGICAL ACTION OF TOBACCO AND ITS ALKALOID, NICOTINE.

Every smoker, almost, remembers the effects produced by his first use of tobacco, and, if he used it in large quantities the first time, he must also remember the horrible nausea, and perhaps

vomiting, from which he suffered. He will probably remember the giddiness and general relaxation which came on, and perhaps he had a sensation bordering on that of suffocation. Be this as it may, the writer thinks he is safe in asserting that every smoker has, at least, suffered some pang, either great or small, after his first use of tobacco, when he has used the drug in the form of smoke. When the drug is "chewed" for the first time, the symptoms are more apt to be severe than when it is smoked. The reasons for this are, that the novice is very apt to swallow more or less of the saliva which has been poured out, and which he has saturated with the various properties of the tobacco. Besides this, much of the drug must be absorbed by the mucous membrane of the mouth. When small quantities are swallowed, the symptoms resemble those produced by smoking, but if the amount has been larger, a very serious train of symptoms arise, which are very apt to end fatally, unless relief is obtained. There is faintness, vomiting, burning in the stomach, purging, increased flow of urine, as regards quantity, and also, often, incontinence of urine and of the fæces. The pulse is rapid and running, and almost imperceptible, even in the larger vessels of the extremities. There are cramps in the limbs, followed by loss of muscular power; the sufferer is covered by a cold, clammy sweat; delirium soon sets in, which is followed by collapse, ending in death, due to failure of respiration.

The action of the pure alkaloid Nicotine is identical with that of the whole drug, except that its results are more rapidly reached, owing to the poison being perfectly free to act as soon as ingested. In cases of poisoning by either the drug or its alkaloid, Nicotine, the prognosis is more favorable if the patient vomits. This is a good sign, because, by vomiting, the patient rids himself of a portion of the poison, and also because it proves that his system is not so absolutely overcome by the poison as to prevent its attempting to throw off the offending agent. Vomiting in such cases is of use in an indirect way, as having a tendency to prevent the patient falling into a soporose condition, in which he is liable to die from failure of respiration, while if

he be awake, he can aid respiration by his will power. Sometimes there are clonic spasms, which do not occur when the case is rapidly fatal.

Dworzak and Heinrich,[1] associates of Schroff, and also Reil, made several experiments with Nicotine on their own persons. The doses they used varied in amount from $\frac{1}{32}$ drop to $\frac{1}{16}$ drop in one drachm of water. The smallest doses occasioned a burning sensation in the tongue, a hot, acrid irritation in the fauces, and when doses somewhat larger were used, the entire length of the œsophagus felt as if it had been scraped by an iron instrument. A sense of heat diffused itself from the stomach to the finger tips, accompanied by general excitement. Still smaller doses occasioned headache, and a sensation as of an aura in the upper jaw. Larger doses implicated the brain, causing torpor, giddiness and sleepiness; indistinct vision, which was nevertheless attended with unusual sensibility of the eye to light; imperfect hearing, a feeling as if the ears were stuffed with cotton; laborious and rapid respiration, and dryness of the throat. In forty minutes after larger doses, a sense of unwonted debility and weariness came on, the head could scarcely be held erect, the face became pale and the facial muscles relaxed, the limbs became icy cold. This coldness advanced toward the trunk, and faintness came on, with commencing insensibility and loss of consciousness. There were unpleasant feelings in the stomach, with eructations, nausea and vomiting, the last producing some relief. The abdomen was distended, and the bowels were the seat of disagreeable feelings. During this time there was an earnest desire to go to stool, and the expulsion of flatus and of some urine produced great relief. This relief did not, however, last long. One of the experimenters was attacked during the first half of the second hour with peculiar clonic spasms of the whole body, which increased in violence during forty minutes, and lasted for an hour. The spasms began by a tremulous movement of the limbs, and gradually extended over the whole muscular system, chiefly affecting the muscles of

[1] Mat. Med. du rein. chem. Pflanzenstoffe, p. 234, quoted by Stillé.

respiration. There was oppression and gasping, every respiratory movement being composed of a number of short and incomplete inspirations. The other experimenter, during this time and at this period of the operation, was affected with unusual muscular relaxation, very laborious breathing, and a rigor. In other respects his symptoms were the same. Both persons, on their return home, felt extremely weak, walked with uncertain steps, and were very chilly; one of them had a return of the spasms and a frequent desire to urinate, which, when gratified, resulted in a copious[1] discharge. The following night both were restless and almost sleepless, and the next day were still unwell, unable to apply the mind, tired, sleepy, and without appetite. The pulse continued weak and irregular, and three days elapsed before the effects were entirely dissipated.

There is one point which the writer forgot to mention when describing the symptoms of Nicotine poisoning, namely, the protrusion of the eyeball and the drawing up of the same, in a spasmodic manner, toward the outward corner of the orbit. This is so great, sometimes, as to hide nearly the whole cornea.

The post-mortem changes, after Nicotine has been the lethal agent, are—great congestion of the various viscera, a peculiar congestion and ecchymosis of the skin, congestion of the conjunctiva, brain and membranes. The heart is found relaxed and flabby, and the right side full of blood. The liver is congested, and the lungs are almost black in color, so great is their congestion. This congestion is due to the death by asphyxia.

In the frog, just before death, there is a convulsive drawing up of the hind legs over the back, and the fore legs are drawn close to the sides and toward the hind legs. This condition is present after death, unless the batrachian be disturbed. That

[1] Although the drug was given in almost a poisonous dose, and, therefore, the result can hardly be called proof of the general action of tobacco in increasing the quantity of urine or the reverse, it seems to the writer that this, at least, favors the assertion made near the beginning of the article, that tobacco does increase diuresis.

is to say, the frog dies in that position and resting entirely on his belly.

Nicotine, notwithstanding its great toxic powers, has been used very rarely as a tool for murder or suicide, probably because it has been difficult to obtain it, and also on account of the general ignorance in regard to its poisonous action. The celebrated case of Count Bocarmé figures almost as an unique occasion on which it was used to commit murder. This case occurred in Belgium, in 1851, the murderer being the Count, who was tried, convicted and executed, for the murder of his brother by forcing the poison down the latter's throat.[1]

So far as the writer can find, there have been but two cases of suicide produced by the alkaloid, one of which is reported by Mr. Taylor, and the other case occurred at Cherbourg, in 1859. While so few cases of a criminal nature have been due to Nicotine, literature on the subject abounds with any number of cases of poisoning, either partial or complete, where accident or ignorance were the exciting cause.[2] The writer once saw a case of this kind while traveling on a train in the West. A child, about two years of age, belonging to the family of an emigrant, succeeded, while the parents' attention was diverted, in obtaining a plug of strong chewing tobacco, and had swallowed quite a large piece before it was discovered. The child did not vomit at all, but seemed to succumb immediately to the poison. The face grew pale and drawn, then clammy to the touch and relaxed. Soon after, the whole body became limp and powerless. The pulse grew rapid and feeble, and the child seemed to be at death's door. There were no convulsions or spasms, but there was forcible ejaculation of urine. The party left the train soon after, and the writer does not know whether there was a fatal ending or not.

Dr. W. J. Tyrrell, of Ohio, reports the case of a healthy little girl who, three weeks previously, fell against a stove and burned

[1] Annales d'Hygiene, 1861, ii.

[2] The writer means here to include those cases due to tobacco itself, as well as its alkaloid.

and bruised her lip. The mother placed the oil out of the stem of a pipe on the lip, to heal it. The child died in the course of a few hours, in violent convulsions.

Husemann states that no less than ten fatal cases have resulted from the use of tobacco enemata alone.[1] Dr. Tavignot records a case where fifteen grains of tobacco were given to a robust man of fifty-five, as an enema, with a fatal result.[2] Dr. Copland has seen a clyster containing half a drachm produce death.[3] Stillé, also, mentions a case in which a strong infusion of tobacco, given as an enema for tapeworm, caused death immediately. In another case, the same result took place in about fifteen minutes, and in a third, in three-quarters of an hour. Mr. Skae reports a case in which a man swallowed a large mouthful of tobacco by mistake. He suddenly became insensible, motionless and relaxed, with contracted pupils and a scarcely perceptible pulse. After these symptoms came loud cries, and dilated pupils, active vomiting and purging. Death, from syncope, finally occurred.

The *Lancet* for March, 1879, p. 296, contains an interesting account of a case of tobacco poisoning, which is here quoted:—

A woman, aged forty, suffering from varicose veins in the leg, struck her leg against a sewing machine. A severe hemorrhage followed, and she attempted to control it by a tight bandage, under which she placed some tobacco. In three-quarters of an hour she appeared dangerously ill, and Dr. O'Neil was called in. He found her prostrated and with all the symptoms of tobacco poisoning, which have been so often repeated that the writer does not think it worth while to burden the reader by again mentioning them.

It was not until Dr. O'Neil removed the bandage that he found the cause of the symptoms. He then washed the wound free of the drug, administered stimulants, and the woman recovered.

[1] Handbuch der Toxicologie, vol ii, p. 483; quoted by H. C. Wood.
[2] Stillé's Therap., Mat. Med., vol. ii, p. 377.
[3] Dict. of Pract. Med.; art. "Colic."

A smuggler,[1] desiring to escape the customs, covered himself from head to foot with tobacco leaf, which, being dampened by perspiration, almost caused his death, by the absorption of the poison through the skin.

An American writer states that soldiers during the war of 1812, when on hard service on the Canadian frontier, frequently disabled themselves for duty by applying a wet leaf of tobacco to the armpit.[2]

A man suffering from piles was advised to sit on a chamber, in which was half an ounce of tobacco and some hot coals.[3] After a few moments he fell to the floor, without any sign of life except a deep sigh, every fifteen or twenty seconds.

Three children had their heads rubbed with an ointment of tobacco. They were suddenly attacked by vertigo, excessive vomiting, fainting and sweating, and for twenty-four hours staggered about like drunken men. Another case, corresponding somewhat to this, is reported by Dr. Truchess, in which some snuff was put on a girl's head for the cure of tinea favosa. In eight or ten hours symptoms of poisoning came on, and the child just escaped death.

A man and his wife were troubled with itch, and, for the purpose of curing the same, rubbed themselves from head to foot with a decoction of tobacco; dangerous and alarming symptoms soon came on, and they were saved, with difficulty, from death.

Murray gives an account of a young man who smoked twenty pipes of tobacco, on a wager, and then fell into a lethargic condition; and also an account of two brothers, one of whom smoked seventeen and the other eighteen pipes of tobacco, which caused death in a manner resembling apoplexy.

A case is related by Marchant, of a smoker who accidentally dislodged a piece of inspissated tobacco juice from his pipe,

[1] Stillé, Therapeutics and Mat. Med., vol. ii, p. 374.

[2] An Essay on the Influence of Tobacco on Life and Health. By R. D. Mussey, M.D. Boston, 1836.

[3] Am. Jour. Med. Sci., Jan., 1847.

which he swallowed. Soon afterward, the man fell down insensible, and would have died if assistance had not been rendered.[1]

Ramazzini saw a girl present all the symptoms of tobacco poisoning and discharge blood from the bowels, from being too long among tobacco bales. Fourcoy states the case of a man who died in *convulsions* from the same cause.

It has been claimed, with only partial truth, that many very serious disorders, not only functional, but also organic, arise from the use of tobacco in any form. The assertions of the older writers are, that cancer is one of the most frequent results of smoking or chewing tobacco, that is, among those diseases which are classed as organic. These cases of tobacco cancer, if the writer can use such a term, are generally connected with some part of the mouth; at least, the writer can find no record of any case of cancer occurring elsewhere when caused by tobacco excess. The word "excess" is used here, not in its generally accepted sense, of intemperance, but in the sense that any luxury which causes pathological effects, be the dose large or small, is in excess of what the smoker, etc., should use. While the older writers generally believed that cancer of the mouth was caused directly by the tobacco, modern authors rather regard the pipe stem as the offending party.

Mr. Lizars, one of the most vehement of anti-tobacco writers, mentions several cases, occurring in his own practice, of carcinoma involving the whole mouth,[2] in distinction from the form occurring solely in the lip. He also quotes numerous other cases from the practice of Mr. Solly and others, of the same character. Many of them occurred in those persons who smoked nothing but cigars, or, rather, never used a pipe. Thus, he reports the case of an East Indian sea captain, whose velum, pharynx, tonsils and left cheek were carcinomatous, who always smoked cheroots, and Mr. Lizars attributes all this to the use of tobacco in this form. With the exception of the cases quoted by Mr. Lizars, the writer

[1] Brit. and For. Med.-Chir. Review, April, 1866, p. 543.

[2] The Use and Abuse of Tobacco. Edinburgh, 1859.

can find no record of such cases reported by other writers. Many surgeons in this country go so far as to state that the disease never appears after the use of tobacco, unless the tobacco be used in a pipe;[1] while others think that tobacco cancer is due to the pipe and the tobacco combined. To the writer, the latter opinion seems the most moderate and probable. So far as the writer can discover, no case of carcinoma of the MOUTH has been reported in this country as resulting from the use of tobacco,[2] while epithelioma of the lip is almost daily met with, arising from this cause.

A paper of this kind is not a suitable place for a discussion as to the pathology of cancer in regard to the hereditary tendency or local origin theories, but it is suitable that the question of carcinoma[3] of the lip and its causes should be considered. Prof. D. Hayes Agnew says, in regard to the causes of epithelioma of the lip:—"Little importance is to be attached to the alleged influence of the clay pipe used in smoking as a cause of this affection, since the number of cases, as compared with the number of smokers, is too insignificant to give the least credibility to this view. It must not be overlooked, however, that the lower lip is much more exposed to irritation from a variety of causes than the upper lip, and this fact may play no inconsiderable part in the causation of the disease."[4] The same author, however, in speaking of the causes of cancer simply as regards its pathology, and reviewing the so-called "inflammatory," emotional and hereditary theories, says:[5]—"The inflammatory theory, which has already been noticed as a cause of carcinoma, is again attracting no small degree of attention, and it is highly plausible that a process of this nature, or any local irritation, may be actively concerned in inducing the disease. Cancer of the lip,

[1] In other words, attributing the entire fault to the pipe stem itself.

[2] Since writing this, the whole country has been grieved and distressed by the progress of just such a case, in the person of General Grant.

[3] Carcinoma and epithelioma are used synonymously.

[4] The Principles and Practice of Surgery, by D. Hayes Agnew, M.D., LL.D., vol. ii, p. 894.

[5] Agnew's Surgery, vol. iii, p. 656

no doubt properly referred to the irritation of the clay pipe in smokers, is an example in point, as females rarely suffer from the disease in this locality. Yet carcinoma occurring in this way by no means establishes the local origin of the disease; rather the reverse, as epithelioma of the lip, compared with the number of pipe smokers, is exceedingly uncommon, and this very fact would seem to imply that without some predisposition of a general character, the local irritation would be powerless to evoke the disease." A little further on, the author quoted says:—"Epithelioma is more frequently observed in males than in females. It is stated by Dr. Marsden, that of 1467 cases of cancer admitted into the Cancer Hospital in London, 1022 were males. Koch, in an analysis of 145 cases, found 132 in males and 13 in females." Dr. Partsch,[1] in analyzing 570 cases of epithelioma, finds that of this number 98 were on the lips, 88 of which were in males and 10 in females. He also asserts that tobacco smoking had little influence in their production, most of them originating in a wound. On page 658,[2] Dr. Agnew again says:—"That much importance is justly attached to local irritation as a cause of the disease, as the contact of the clay pipe or a sharp tooth in carcinoma of the lip and the tongue." Dr. Ashhurst says,[3] speaking of epithelioma:—"Inheritance is rarely traceable in this form of the disease, while a large proportion, probably a majority, of cases appear to have originated from a local cause or injury. Thus, epithelioma of the lower lip is often attributable to the habit of smoking a short pipe; in the tongue, the disease may originate from the irritation caused by an uneven tooth." Prof. Louis Duhring,[4] speaking of the same disease, says:—"The exciting causes are often obscure. The disease is apt to have its starting point in a locally irritated tissue, as, for example, in an excoriation, or about a lip that had been irritated by the use of the pipe, or through uncleanliness."

[1] Phila. Med. Times, April 4, '85. Transactions.

[2] Agnew's Surgery, vol. iii.

[3] The Principles and Practice of Surgery, p. 506.

[4] Diseases of the Skin, 3d ed., p. 552.

Butlin says:—"The habit of smoking undoubtedly predisposes to the formation of epithelioma of the lip, and it is a remarkable circumstance that more than one of the few women who have suffered from this disease have been habitual smokers."[1]

Prof. S. D. Gross mentions the use of a pipe as a possible exciting cause of epithelioma of the lip.

Although some of the opinions expressed on one or two occasions, by the various writers, have not been as clear or decisive as might be desired, still the mass of opinion favors the conclusion that epithelioma of the lip MAY be caused by the use of a *pipe* in smoking, and this conclusion does not interfere with any of the theories concerning the formation of cancers. These theories do, however, interfere with the conclusions which one would like to draw, very seriously. If cancer is likely to occur only in those who have a hereditary tendency or diathesis, then the danger of using a pipe in smoking is almost necessarily confined to this class.

On the other hand, if the inflammatory theory is true, the danger from the tobacco pipe is one to which every pipe smoker is exposed.

Be this as it may, it is evident that many circumstances are present when a pipe is used which would prepare a good field for the malignant growth to start in. First, the pipe stem, which, by its pressure on the lip, tends to stimulate the formation of new epithelial cells; second, the fact that the saliva naturally has a tendency to flow over the most depressed portion of the lip which is depressed by the weight of the pipe; third, that this saliva macerates the tissues around the pipe, thus enabling the stem to irritate the lip without great motion or force; and on top of all this what might be called "fertilizing," if the writer can use such a term, comes the irritating smoke, containing the sulphide and cyanide of ammonium, and the still more harmful and acrid Nicotine. The saliva, too, while causing the macera-

[1] International Ency. of Surg., art. "Tumors," by Henry Trentham Butlin, F.R.C.S.

tion, contains a certain amount of the Nicotine, which has been precipitated by losing its heat.

Many men, too, who smoke a pipe, chew; and thus you have about as constant a source of irritation and maceration as can well be imagined. When we consider all these predisposing causes to cancer, we can hardly help believing that cancer of the lip would be far more common among pipe smokers if the inflammatory theory of the disease was entirely true, and there was no cancer diathesis to be a factor in the formation of the affection. Whatever may be the real danger of using a pipe for smoking, it certainly seems probable, at least, that the danger of cancer of the lip is not so great when the cigar or cigarette be used, although other dangers may exist, due to greater quantities of Nicotine being inhaled in the latter case than in the former. There is one danger which those who use a pipe may be exposed to, namely, *syphilis.*

Although the transfer of the pipe from one person to the other, *while smoking*, is more common among the lower classes than among the upper, it is not an infrequent thing to see one man using another man's pipe; and particularly is this so among men in colleges and clubs. Why is it not possible to be inoculated with syphilis by putting your lips to the same mouthpiece which another man with mucous patches in his throat has had in his mouth? Why should not the second smoker, by the suction required in smoking, draw into his mouth some of the saliva which his predecessor allowed to escape into the pipe stem? This subject has been written on quite extensively by Prof. Sigmund, of Vienna, but the writer has been unable to find the original paper.

Mr. Lizars, speaking of this subject, says:—"I have been often consulted by gentlemen having syphilitic sore throat which they could not account for, having had no primary symptoms[1] on the genitals. On interrogating them, they have admitted using a pipe of another, or having accepted a puff of a friend's

[1] Loc. cit.

cigar. Some patients have presented themselves with syphilitic ulceration on the lower or upper lip, or the commissure between them having a thickened base. Some have had syphilitic ulcers of the mucous membrane of the cheeks, tongue and tonsils."

When we consider how widespread this disease is, affecting all classes, we can but wonder that more cases of the kind just mentioned are not reported. Very few cases are recorded, comparatively, of persons who have the "initial lesion" on the lip, or elsewhere than the genitals;[1] and it seems to the writer that in cases where no history of illicit intercourse or like exposure to syphilis can be discovered, it would be well to question the patient as to his habits as regards smoking another's pipe, or taking a chew from a borrowed plug of tobacco. If this plan were carried out, would not many obscure histories of syphilis be made clear and the patient's denial of *illicit intercourse* be accepted as a truthful statement? It has been claimed that angina pectoris is a frequent result of excessive smoking. It is probable that smoking only brings on this condition when the person is one of a nervous temperament, and thereby easily falls a victim to the nerve-disordering drug.

Dr. Corson, in the half-yearly abstract of the *Medical Sciences* for the first six months of 1854, records a case of this kind, and also reports the entire cure after the withdrawal of the "weed." The disease is one which, of itself, is quite rare, and must be seldom the result of tobacco. Many of the text-books do not mention tobacco as a cause, at all, of this disease.

Passing on to minor troubles, we find that almost every constant smoker suffers from catarrh of the nasal passages, or else pharyngitis. Frequently the smoker complains of a constant tendency to hoarseness on the slightest exposure; in other words, he suffers from chronic laryngitis. Ophthalmia and amaurosis are frequently seen in the smoker, and the well-known ophthalmologist, Sichel, held the opinion that few persons *smoking* five drachms of tobacco a day for a long period

[1] See Report of Ten Cases of Extra-Genital Chancre, with Remarks. Phila. Med. Times, Nov. 1, 1884.

escaped from diminution of vision. The opinion of Sichel is not coincided with by all other writers, however. Ophthalmologists on the Continent do not believe in tobacco amaurosis, while Crichett and Hutchinson, with others, firmly believe in the disease, regarding the condition as one form of atrophy of the optic nerve. While the subject of tobacco amaurosis may be one of dispute, it certainly is a fact that failure of vision, characterized by an indistinct view of objects, is often seen in those who are intemperate smokers or drinkers. In such cases as those first mentioned, the ophthalmoscope shows nothing but undue vascularity and slight opacity of the optic disk.

The most common effects of smoking and chewing are seen in those cases of cardiac palpitation, or "tobacco heart," as it is sometimes called, and also in those persons using the drug for chewing who suffer from a variety of chronic indigestion.

It is probable that the palpitation is brought about, not by a direct action of the drug on the heart, but by a condition of nervous irritability, which may only affect the nervous system in that region, to all appearances, although the rest of the nerves are really involved. Of course, indigestion can be brought about by smoking as well as chewing, by depressing the nervous system. The habit of chewing, however, affects the digestion much more directly. It causes an undue pouring out of saliva into the mouth, which is either swallowed as a saturated solution of tobacco or ejected, and as a consequence the food, when masticated, is deprived of its ptyalin, to a certain extent, as well as the complete moistening which is so necessary to perfect digestion. The drug comes in direct contact with the mucous membrane, which absorbs substances with great ease, and if the saliva, as before stated, be swallowed, the man virtually takes poison into his stomach all the time. Darwin, in his "Zoönomia," vol. ii, p. 701, says:—"The unwise custom of smoking and chewing tobacco for many hours a day, not only injures the salivary glands, producing dryness of the mouth when this drug is used, but I suspect that it also produces scirrhus of the pancreas. The use of tobacco in this immoderate degree

injures the powers of digestion, by occasioning the patient to spit out that saliva which he ought to swallow, and hence produces that flatulency which the vulgar often take it to prevent."

As far back as 1622 Mourach, the Sultan, prohibited the use of tobacco, on the score of its anaphrodisiac effects. Mr. Solly, the well-known surgeon, says, in the London Lancet of February 14th, 1857, that tobacco, when used immoderately, extinguishes the sexual appetite, and annihilates the reproductive power. He thinks it is a frequent source of "spermatorrhœa," and goes on to say that in one week he had been consulted by three young men suffering from seminal weakness, and that in each case he could trace the trouble to the use of tobacco. It is probable that in all such cases as those just mentioned, the lack of power and the so-called spermatorrhœa are the result, not of the drug's use directly, but rather of the condition of nervous irritability and depression of the vital forces brought about by excessive smoking or chewing.

If all the diseases mentioned be grouped in the reader's mind, and if he will go still further, and regard carefully the accounts of cases spoken of, even by anti-tobacco writers, the writer is confident that the following points will be observed:—

First, that in all cases where evil results of any consequence came about, the drug had been "*always*" used in "*excess*" or "*immoderately.*"

Second, that these serious cases, when they did appear, were exceedingly rare and far apart.

Third, that most of the cases reported were put on record at a time when anti-tobacco feeling ran very high; and although the writer does not doubt that in every case the diagnosis was correct, it at least seems probable that cases were reported as the result of smoking, etc., which were really due to other causes.

There are certain troubles, however, which really do follow the use of large quantities of tobacco, and although they have already been mentioned, it may not be out of place to bring them once more before the reader.

They consist chiefly in dryness of the throat, indigestion,

laryngitis and pharyngitis and nervous irritability. The latter trouble manifests itself in various ways, according to the temperament of the person. Of course, the chief method of cure in such cases is the prohibition of tobacco in any form.

When we consider the vast number of the human race who use tobacco, and the enormous quantity[1] which they consume, we can hardly avoid coming to the same conclusion as Dr. Anstie,[2] that while the use of tobacco is in some cases highly injurious, in others it has very little effect. To the young, especially, tobacco is a perfect curse, stunting their development, injuring irreparably their general physique and growth, and often entirely altering their dispositions by bringing on a state of constant irritability. Its use is to be condemned in those of a sanguine or nervous temperament, and to be at least "winked at" if not approved of, in those whose temperament is more phlegmatic and less easily disturbed. The writer even goes further than this, and asserts that to the aged, who by long use have become accustomed to the drug, it is an actual necessity, for health or happiness. Withdraw for one day the accustomed smokes of an old man, and see how miserable he becomes. This is not entirely a feeling brought about by mental desire for the drug, but because his system must have its accustomed dose of tobacco. The writer knows an old man, personally, who after being out for a few hours will come in to his house, pale, feeble and exhausted; so nervous, too, that he can hardly articulate, but who becomes quiet and comfortable after a few draws at his well-beloved pipe. To the laborer or the man whose avocation keeps him out of doors, it is probable that tobacco rarely does harm, and in cases of great physical fatigue is often of use, calming the restlessness so often present after a hard day's tramp in the open air.

To the man of business, who is confined to an office and desk all day, to the hard student or the sickly, tobacco is decidedly harmful, and although the student often smokes with the idea

[1] For some interesting tables in regard to the amounts of tobacco produced, its average value, etc., see Appendix.

[2] Stimulants and Narcotics.

of inducing sleep, he seldom obtains it, unless in a form of stupor, which does not resemble the hypnotic effects of a good, brisk walk before going to bed. Willis, in his "Practice of Physic," written just two hundred years ago, in 1684, says of the hypnotic powers of tobacco:—"It doth not only procure sleep alone, but sometimes, also, the contrary of sleep, which is watchfulness." After all, the whole question of tobacco use depends upon the quantity consumed, and the user of tobacco must gauge his use of the "weed," not by the amount which another man can stand without harm, but by the power which he finds the drug can exercise in his own person. Moderation is not the use of a small quantity of tobacco, but the use of such a small quantity that its results are not serious.

It is the argument of many, that it is impossible for one to grow so accustomed to the action of a drug containing such a powerful alkaloid as Nicotine without harm.

To these the writer replies, that the human race can become habituated to any poison, never mind how deadly, provided it be given in *moderate* quantities. The Styrian peasant can devour enough arsenic, without other than good results, to kill several ordinary Europeans. The opium eater can consume enough opium to narcotize several average men. Haschisch, or Cannabis Indica, is used by the Eastern nations *most extensively*.

To this evidence the argumentative reader will say, that the evil effects of opium and haschisch are notorious, and that by mentioning them for the purpose of maintaining that the use of tobacco, by analogy, is not harmful, the writer has made an egregious mistake.

To this he replies:—Certainly opium and haschisch, and tobacco, too, for that matter, are capable of producing great evils if they are *used* in excess, but not if moderation, of a strict type, be adhered to. After all, tobacco is only one of the numerous luxuries with which mankind enjoy themselves, and coffee and tea have probably produced an equal number of victims.

Caffein, the active principle of coffee, is capable of producing very serious toxic effects if given in large doses, and is a drug

which stimulates the heart and disorders the nervous system far more frequently than the coffee drinker dreams of. It produces undue mental activity when such activity is not desired. If this mental activity be increased by additional doses of the drug, the patient will pass into a form of delirium. An eminent writer on therapeutics expresses so exactly, in writing on caffein, what the writer desires to express with regard to tobacco, that the liberty is taken of copying his words *verbatim:*—

"The enormous use made by mankind of substances containing caffein, indicates that in some way it is directly of service in the wear and tear of daily life. It is not probable that any of the caffein is assimilated, but it may be considered established that it checks very greatly the elimination of nitrogen, or, in other words, lessens the waste of tissue."

On the same ground, the writer considers that the enormous use of tobacco is also produced by the instinctive desire for some article which will retard tissue waste. Indeed, all drugs which prevent the excretion of nitrogenous material have been sought after, since the earliest history of man, and we can be pretty sure that a drug which is used everywhere and by everybody is one which helps a man to stand the jar and worry of business or other pursuits.

Tobacco, coffee, alcohol, all retard tissue waste, and, therefore, men, women and children long for them, and, from using them instinctively and for a purpose, they soon use them in excess and as a luxury. Dr. McPherson,[1] quoted by Stillé, testifies in regard to the use of opium in moderation, as follows, and, as he mentions the use of tobacco, it may be permissible to bring his words before the readers of this paper:—

"Were we," he remarks, "to be led away by the popular opinion that the habitual use of opium injures the health and shortens life, we should expect to find the Chinese a shriveled, and emaciated and idiotic race. On the contrary, although the habit of opium smoking is universal, amongst the rich and poor, we find them to be a powerful, muscular, and athletic people,

[1] "Two Years in China;" quoted in Bell's Bull. of Med. Sci., 1843.

and the lower orders more intelligent, and far superior in mental acquirements to those of corresponding rank in our own country."

"The opinion of the Chinese regarding opium is very much like that of many in our country regarding tobacco, and proves that it would be as unfair to deduce the effects of opium eating or opium smoking from those produced by the drug in medicinal doses upon persons unaccustomed to its use, as it would be to expect, from the habit of chewing or smoking, the violent and even poisonous effects which tobacco sometimes produces when administered by the rectum, in cases of strangulated hernia, or when first ventured on by boys who imagine that it is manly to ape the vices of men."

ACTION ON ANIMALS.

Schubarth made twenty experiments upon the horse,[1] giving four ounces of powdered tobacco to each animal, and found that the pulse-rate was decreased from thirty-seven to twenty-seven per minute, and that this depression lasted twenty-four hours. Sir Benjamin Brodie[2] found that an infusion of tobacco, (the amount not stated) injected into the rectum of dogs, caused the animals to become insensible, motionless, and all died in less than ten minutes. The pulsations of the heart were not present, so he states, for a minute before death.[3] Vomiting occurred in only one case. Brodie likewise performed the same experiment upon cats, with like results. Mussey[4] states the case of a horse which was killed by the injection into the stomach of an infusion of tobacco and also that of a calf, who, being washed with a tobacco infusion, for the purpose of killing vermin, died in consequence.

[1] Horn's Archiv, 1824.

[2] Orfila: General System of Toxicology, 1817, vol. ii, page 211.

[3] There is probably some fallacy underlying this statement of Brodie's, since all other observers, including the writer, mention the heart's beating some time after the stoppage of respiration.

[4] An Essay on the Influence of Tobacco on Life and Health. By R. D. Mussey, M. D., Boston, 1836.

Dr. Murray states that frogs placed in a jar containing tobacco smoke became soporose, panted, and finally died. He also killed a sparrow and a magpie in the same manner.

The writer performed the same experiment on the frog, the principal symptom noticed being an absolute relaxation of the whole body, so that the batrachian lay prone on his belly, with his limbs limp and powerless.

Several experiments were likewise performed by Mussey on rats and cats, the distilled oil of tobacco being used. He found the rats were less affected by the poison than the cats, and that the younger the animal, the more rapid the toxic effect.

In 1846, Wright, of Birmingham[1] (England), found that when two to five grains of the essential oil of tobacco was given to dogs two or three times a day, gradual and complete marasmus came on, accompanied by a dragging of the hind legs, loss of sexual power, shriveling and softening of the testicles, shedding of the hair, and later on, sloughing of the eyelids and blindness. The post-mortem lesions consisted in fluidity of the blood, which was deficient in fibrin and was lacking in red corpuscles. The heart was pale, small and soft. Rigor mortis never came on, and decomposition rapidly ensued. Before the experiments were fully under way, the gums became sore and bleeding; often the teeth dropped out. The mucous membranes of the mouth and air passages were tumid and more vascular than normal.

An account is given of a black snake into whose mouth was thrown some tobacco juice. The reptile writhed in spasms for a short time and then died.[2]

M. Melier performed many experiments on dogs and cats with Nicotine, which he injected subcutaneously, in doses of from five to eight drops. The breathing was, in most of the cases, affected first, and was noted as difficult and anxious; the pupils were dilated, and the animals staggered in their gait; violent efforts at defecation came on, with a copious discharge of "urine, ap-

[1] Am. Jour. Med. Sci., Jan., 1847.

[2] Boston Med. and Surg. Jour., Oct., 1856, p. 216.

parently followed by relief; at a point further on there was vomiting, trembling, and in some instances, a rapid movement of the ears, with frothy mucus running from the mouth."

"When death occurred, it was preceded by signs of complete exhaustion, and more remotely, by convulsions. The exhaustion and convulsions appeared to affect the hind legs chiefly."

The writer injected[1] $\frac{1}{32}$ drop of Nicotine into a full-grown rabbit, and in a short time the animal became restless, followed, in an instant, by great quietness, and evidently, an inability or disinclination to move. This was followed, shortly after, by a rapid hopping around the room, accompanied by the expulsion of urine with sufficient force to send the liquid over the floor for at least two feet from the rabbit; there was defecation, followed by the animal toppling over and dying, evidently from failure of respiration, the time between the administration of the drug and death being about five minutes.

PART FIFTH.

THERAPEUTIC USES AND EFFECTS OF TOBACCO.

In considering the use of tobacco as a therapeutic agent, we must be prepared to act as critics of the array of facts brought before us, and try to decide whether its advantages are greater than its disadvantages, or *vice versa*. The chief reasons against the use of the drug in medicine are as follows:—

First. Its virulence as a poison.

Second. Its general effects on the whole system as well as on the part of the system which we desire to affect.

Third. Its nauseating odor to some people.

Fourth. The difficulty in obtaining a uniform strength in the crude drug.

Fifth. The unexpected and insidious action of the drug on those who, by idiosyncrasy, are not fit subjects for its use.

[1] Subcutaneously.

In regard to the excessively poisonous properties of tobacco, we can only stop for one moment and consider that many of the drugs in use every day are just as poisonous, if not more so, and that idiosyncrasy governs their administration more closely than that of tobacco, in many cases. The writer does not think it just that a drug should be professionally tabooed solely because of its poisonous qualities, and he thinks that the reader will certainly, in this respect, agree with him. Many of our most potent and useful drugs are poisonous in far smaller doses than even the pure Nicotine, and many of them, too, kill, by acting as heart depressants. Once stop the heart by a poison, and the man dies; but depress or stop respiration, and artificial and external measures can be easily undertaken which will supply the necessary air for life. Let us consider as proven, therefore, that as far as its poisonous properties alone are concerned, tobacco may be considered as a useful member of our Pharmacopœia.

The second reason against its use is far more forcible than the first, and might be considered strong enough to entirely prevent its use, provided that some other drug could be used with equally advantageous, or partially advantageous, results. Given a case of threatened asthma in a woman, or one unaccustomed to smoking, and give as a cure for the threatened attack a strong cigar, and you ward off an attack of asthma, only to throw your patient into a condition so utterly miserable that she would gladly stand her asthma, thinking the remedy worse than the disease. You would bring on a great nausea and a feeling of general malaise, and, perhaps, dangerous vital depression. It is impossible to limit the effects of tobacco to any one portion of the body; and while this may be true of other drugs, still, many of them do not produce the unpleasant symptoms caused by tobacco.

The general characteristics of a drug are really important factors in their use, very frequently. It is a generally understood fact among practitioners that the old Misturæ Diabolicæ of our forefathers, while often potent and efficient, formed a stepping stone for such dogmas as homœopathy and kindred sugar-coated infinitesimals.

This is certainly so as regards children, for parents dislike forcing their children to take doses which they themselves regard only as horrible alternatives, and they are ever ready to believe that as long as a medicine tastes good, it is better than that which is otherwise.

The medical practitioner who prescribes ever so wisely and appropriately for a patient, but who is utterly regardless as to his combinations of drugs, as far as taste is concerned, will, sooner or later, see a more ignorant man take from him that practice which his greater wisdom entitles him to, but which is driven from him by his own mistake in this matter. While in some cases there is no alternative but to give a bad dose, in the subject before us we find many alternatives, or rather substitutes, for tobacco, whose powers as depresso-motors are fully as great, and far less disgusting and repulsive in their administration and effects.

The difficulty in obtaining the drug with a uniform strength is one which militates strongly against its use. The difference in the proportion of its active principle being very great, according to the variety used; and even if a particular kind of tobacco was ordered for the preparation of the officinal article, it is probable that other varieties would soon creep into the drug store.

Idiosyncrasy on the part of the patient has already been touched on. While it is true that other drugs, in their administration, are governed by the peculiarities of the patient, it should not be forgotten that the drug is so largely used as a luxury, that in certain cases the most heroic doses would have no effects, while to a person not accustomed to the action of the drug, comparatively minute doses would be followed by dangerous consequences. The action of the remedy is so sudden and insidious, that no amount of care could prevent accidents, which would test the best talent of the physician to overcome. Although tobacco was at one time considerably used for various purposes in medicine, it has, at the present day, fallen out of professional favor. That this disuse of the drug has been de-

served seems proven, both by what has just been said and the array of cases of accidental poisoning which have already been cited. However this may be, it is interesting and instructive to recite briefly some of its former uses as a medicinal agent.

Tetanus has probably been the field where tobacco has done the best work, at least in combating very serious diseases, since its action is so largely depresso-motor as to preclude its use in any disease but one of extreme nervous excitement. Before more rapidly-acting and less dangerous drugs of a depresso-motor character were known or understood, tobacco stood almost as the sole reliance of the surgeon who had such cases to govern. It seems to have been used equally frequently in both traumatic and idiopathic tetanus, and the results were about as satisfactory in one instance as the other.

Its use in idiopathic tetanus was much earlier than in the traumatic form, and in the latter cases its use was first reported in 1815.

The table on the opposite page shows quite a number of cases in which tobacco was used with good results in both forms of this horrible disease. At first sight, these statistics would, apparently, show that the drug was a good agent in combating tetanus, but it must not be forgotten that the cases in which it was used with no effect are not included in this table, and, as has been said before, other drugs can do the work better and with greater certainty and far less danger. Dr. Curling,[1] in speaking of tobacco in this connection, says, that the full effects of the drug are so peculiarly distressing, that patients often refuse to take any more of the preparation. A dose must be certainly very vile which a man suffering from tetanus would refuse, although it was supposed by him to be his only hope for relief. Mr. Curling found in his collection of nineteen tetanic cases, treated in this way, that nine recovered, and he asserts that in no case where the tobacco was given previous to constitutional loss of power and was fully and fairly tried, was there a single death. He does not state that it is always of avail, but

[1] Treatise on Tetanus. London, 1836.

TABLE SHOWING CASES OF TETANUS CURED BY THE USE OF TOBACCO AND NICOTIA.

No.	Sex and Age of Patient.	Variety.	Nature of Injury.	Mode of Administration.	Duration of Disease.	By Whom, and When Reported.	No. of Cases.	Other Drugs, etc., Used.	Date.
1	.....	Traumatic.	Lacerated foot.	Smoke.	.....	Duncan. Edin. Med. and Surg. Journal, XI, 198.	One.	None.	1815
2	.....	Traumatic.	.....	Fomentations, injections and cataplasms.	.....	Anderson. Trans. Med. Society of Edinburgh, II, 365.	Three.	Purgatives.	1822
3	Female. 40.	Traumatic.	Cupping of temples.	——— Not given.....	.....	Anderson. Trans. Med. Society of Edinburgh, I, 184.	One.	Purgatives.	1822
4	Female. 35.	Traumatic.	Incised wound of hand and fingers.	——— Not given.....	6 weeks.	Anderson. Trans. Med. Society of Edinburgh, I, 184.	One.	Purgatives.	1822
5	Female. 14.	Traumatic.	Lacerated wound of wrist	——— Not given.....	2 months.	Travers, on Const. Irrit., II, 323.	One.	Purgatives and opium.	...
6	.....	Traumatic.	Foreign body in bowels.	Enemata.	.....	Smart. Amer. Jour. Med Sciences, VI, 337.	One.	None.	1825
7	.....	Idiopathic.	.....	.....	6 weeks.	O'Beirne. Dub. Hosp. Reports, III, 343.	One.	.....	1826
8	.....	Traumatic.	.....	.....	.....	Briggs. Dub. Hosp. Reports, III, 343.	One.	None.	1826
9	.....	Traumatic.	Wounded by splinter, hand.	Application of tobacco to epigastrium and wound.	13 days.	Jackson. Med. Record, X, 315.	One.	None.	1826
10	Male.	Traumatic.	Fore-finger wounded by a blunt piece of tin.	.....	A few hours.	Curling. Treatise on Tetanus, London, 1836.	One.	Opium and amputation.	1836
11	Male. 22.	Traumatic.	Gunshot wound of elbow.	.....	6 weeks.	Curling. Treatise on Tetanus, London, 1836.	One.	Opium, stimulants, and warm bath.	1836
12	Male. 14.	Traumatic.	Laceration of hand.	——— Not given.....	13 days.	Curling. Treatise on Tetanus, London, 1836.	One.	Purgatives and leeches.	1836
13	.....	Traumatic.	Blow on the side.	Enemata.	.....	Bulloch. Lond. Med. Gaz., July, 1841.	One.	None.	1841
14	.....	Traumatic.	.....	Enemata.	.....	Predie. Month. Jour. of Med. Science, Mar., 1846; p. 650.	One.	None.	1846
15	.....	Traumatic.	.....	Nicotia, internally; $\frac{1}{12}-\frac{1}{6}$ drop, by the mouth.	.....	Simon. Times and Gazette, July, 1858; p. 112.	One.	None.	1858
16	.....	Traumatic.	.....	Nicotia, internally; 1 drop every two hours, by the mouth.	.....	Haughton. Dub. Quar., Aug., 1862; p. 172.	One.	None.	1862
17	.....	Traumatic.	Severe compound fracture of right radius.	Same as above, and also enema.	13 days.	Tufnell. Amer. Jour. Med. Sciences, April, 1863; p. 496.	One.	None.	1863
18	.....	Traumatic.	Amputation of thigh.	——— Not given.....	.....	Campet. Traite des Mal. graves, 18.	One.	Purgatives and opium.	...
19	Male. 16.	Traumatic.	Compound comminuted fracture of great toe.	Nicotine, $\frac{1}{2}$ – 3 drops every few hours.	5 days.	Morgan. Med Press and Circular, June 2, 1869.	One.	Morphia.	1869

believes it to be the best remedy for tetanus at the time he writes.

M. Cavenne, who wrote on the same subject at the same time, but whose paper was original, in that he was ignorant of the paper of Mr. Curling, reported quite a number of cases of both varieties of tetanus treated in this manner, and in all of which favorable results were obtained.[1] The writer has been unable to see the original report of the article, and, therefore, cannot give any more of the details in regard to cases, except that they were all treated by injection into the rectum.

Mr. Curling (*loc. cit.*) recommends the administration of a sufficient quantity at first to thoroughly impress the system, and that enough of the drug should be given afterward to maintain the effects. He advises the use of a scruple of tobacco leaf made into an infusion by the addition of eight ounces of water for the first dose, and either a stronger or weaker infusion for the other doses, according to the condition of the patient.

As tetanus was combated at one time by tobacco or its alkaloid, it is not surprising that its ally, strychnia poisoning, should have been treated on the same plan, and several favorable results were obtained. Dr. O'Reilly, of St. Louis, cured a person who had ingested six grains of strychnia by the use of an infusion of tobacco, in 1857. In 1862, Dr. Smyly, of Dublin, cured a boy who had taken about four grains of strychnia. In another case, reported in the *British and Foreign Medico-Chirurgical Review*, for January, 1867, a cure was effected by the use of a strong infusion of the drug, although the convulsions were very severe indeed. This case was one of attempted suicide, and the amount of the poison was three grains. Prof. Haughton, of Dublin, performed, in 1856, some very interesting experiments in regard to the antagonistic effects of Nicotine and strychnia.[2] They consisted in placing frogs in solutions of strychnia and Nicotine, and noting the length of time, in each case, before death came on.

[1] On the Employment of Tobacco in the Treatment of Tetanus. Bull. de l'Acad., i, 193

[2] Am. Journal Med. Sci., April, 1857, p. 551.

In other experiments, he placed the frogs alternately in the two solutions, and the latter part of his paper is here quoted:—"In the fifth experiment, the frog lived forty-seven minutes in a mixture of the two solutions, of which one would have destroyed life in four minutes, and the other would have produced paralysis in one minute and destroyed life in three minutes; and yet in the mixture the animal lived forty-seven minutes, and afterward twenty-four hours. In the sixth experiment, the frog, immersed in a similar mixture of the poisons for ten minutes, had ultimately recovered, the effect of the strychnia being entirely obviated by the Nicotine."

In 1877, Haynes proved, very conclusively, that Nicotine and strychnia were not antagonistic, and even went as far as to state that, on the contrary, they were similar in their action.[1] His experiments were made on rats, cats, rabbits and dogs, and were one hundred and forty-three in number. He concludes, from twenty-one experiments, that the minimum fatal dose for a rat is $\frac{1}{150}$ of a drop of Nicotine, the average weight of the rats being about ten and one-quarter ounces. The conclusions which he draws are summed up by him as follows:—

1st. Strychnia and Nicotine are in no degree antagonistic poisons.

2d. Strychnia increases the convulsive action of Nicotine, and does not diminish the motor paralysis of the same.

3d. Nicotine (even in paralyzing doses) increases the convulsive action of strychnia.

4th. Both poisons cause death by paralyzing the respiratory apparatus. They may affect respiration in different ways, but the result is the same.

5th. Animals may be killed by injecting together doses of the two drugs, which, singly, are not fatal.

He then goes on to say:—"It may not be out of place to mention the fact, that experimentation has proven that Nicotine and strychnia show a remarkable similarity in their intimate action on the nervous system, both being excitants of the spinal

[1] Phila. Med. Times, vol. vii, p. 363.

cord and paralyzers of the motor or efferent nerves."[1] Although the writer quoted is certainly right in stating what he does in regard to the similarity of action of the two drugs on the nervous system, it is but fair that the whole state of the case should be given to the attention of the reader. The actions of the two drugs may be summed up briefly and completely in a few words. Strychnia produces convulsions, by stimulating the motor tract of the spinal cord. The convulsions of Nicotine poisoning in the first stage *may* be due, possibly, to temporary excitation of the same tract, but, probably, are due to paralysis of the spinal inhibitory centres in the cord.[2] If the Nicotine convulsions are due to excitation, then the actions of Nicotine and strychnia are identical, but only so in part, since Nicotine goes on and depresses the cord, and strychnia does not do so. If the convulsions of Nicotine are due to the depression of the reflex inhibitory centres, then the *actions* of the two drugs *are different*, but *their effects* are the SAME, in this first stage. Haynes, as already stated, found that the Nicotine increased the convulsions of strychnia. If the Nicotine produces the effect on the spinal inhibitory centres mentioned above, it will readily be seen how Nicotine does increase strychnia convulsions, viz., by paralyzing the only power which could by any chance control the strychnia movements, viz., the reflex spinal inhibitory centres.

Thus it will be seen that in the first stage, although the drugs do not act in the same way, they nevertheless are not antagonistic, but rather aid each other. Later on in the poisoning, by either drug, the motor nerves become paralyzed, but this paresis takes place very late in strychnia poisoning and very early, comparatively, in poisoning by Nicotine.

To the writer's mind, Dr. Haynes' paper proves very conclusively, both by theory and practical research, that Nicotine should not be used as an antagonist to strychnia; that his statement in regard to their both being spinal excitants is

[1] Dr. Haynes refers here, by a foot-note, to H. C. Wood's Therapeutics, in support of his statements.

[2] See Action on the Nervous System.

incorrect, and his statement "that Nicotine and strychnia show a remarkable similarity in their intimate action on the nervous system" is only partially the truth, and is, therefore, calculated to mislead. No one would ever think of classing Nicotine and tobacco with strychnia as excito-motors.

Tobacco has been used in many other diseases than those already mentioned, such as spasmodic asthma, strangulated hernia, ascarides, pneumonia, hæmoptysis, whooping-cough. As usual, it has been claimed that tobacco is a remedy for epilepsy. In dropsies, tobacco would appear to be really efficacious, and a number of favorable results have already been mentioned in this paper.[1] Spasmodic croup, spasm of the glottis and allied troubles have also been treated by means of this agent. The use of tobacco externally is really often of value, and in pruritus it is almost a specific. In various skin diseases, such as urticaria, pityriasis, etc., tobacco has been superseded by more safe and sure drugs. Hemorrhoids have also been relieved, when painful, by *bathing* them with an infusion of tobacco. Applied to gouty and rheumatic joints, tobacco often gives relief, but the dangerous results which may ensue on its absorption should never be forgotten.

Before closing this part of the article, it may be well to give the *treatment* of tobacco poisoning, both in its mild form, such as is seen every day in the small boy, and in its more serious aspect, as the accidental swallowing of some of the poison in large quantities.

The use of ammonia and alcohol internally, and the former held to the nostrils as well, is not only indicated by the symptoms, but also by our knowledge of the action of the drug. The dose should be small and frequently repeated. When the poisoning is sufficiently severe to cause serious symptoms and great alarm, the stomach should be relieved by an emetic or stomach pump. Dry heat should be applied, together with rubbings and artificial respiration. Alcohol, ammonia and digitalis may be administered, the latter hypodermically.

[1] See Physiological Action on the General System.

APPENDIX.

Although the matter contained in this appendix is not, strictly speaking, included in the meaning or aim of this paper, the writer thinks it interesting enough to engage the mind of the reader. It shows the enormous amount of tobacco which this country produces, and also, on the principle of the supply being governed by the demand, the large amount of the drug which must be consumed.

The tables[1] show the value per pound, yield per acre, value per acre, of the crops of 1881, 1882 and 1883, and also the estimated area, product and value of the tobacco crops from 1868 to 1883, inclusive. It will be seen that in 1880 the production was 460,000,000 pounds, which is 120,000,000 pounds less than the year 1877. The census of 1880 showed a population in the United States of 25,417,581 males and 24,632,284 females. Assuming that three-fourths (!) of this number smoke, the remaining one-fourth, consisting of those who do not use the "weed" at all and children who are too young to smoke as a habit, we find that we have to divide a production of 460,000,000 pounds among 19,063,186 smokers. If this be carried out still further, we find that each smoker would consume twenty-four pounds of tobacco per annum, or an allowance of 505 grains of tobacco a day, which would be represented by a little less than seven cigars a day. To be sure, much of this tobacco is, of course, exported, but this is *somewhat* counterbalanced by the importation of foreign tobacco, particularly Havana.

Assuming, again, that tobacco contains, on the average,[2] four per cent. of Nicotine, then in every hundred grains of tobacco we would have four grains of the most virulent of poisons, and the man who smoked 505 grains of tobacco a day would thus be exposed to over twenty grains of the poison, which he fortunately, as before stated, escapes, owing to the volatility and destruction of the poison by the heat.

The question as to whether tobacco is harmful, when used as

[1] See pages 82–85.

[2] See page 14, for Tables of Percentages.

a luxury, has been dealt with so fully already in this paper, that anything further which the writer might add would be superfluous; but it may not be out of place to sum up, very concisely, the evidence and opinions expressed.

Tobacco does *no* harm, when used in moderation—to the man who, by occupation, leads an outdoor life, or one in which much physical exercise is taken, but rather does good, by quieting any tendency to continued action which may exist; to those who, by exceptionally long use, have become inured to the effects of the drug, and whose systems depend on it; to those whose temperaments are naturally phlegmatic and easy going.

Tobacco *does harm* to the young and not yet full grown; to the man of sedentary habits; to the nervous and those whose temperaments are easily excited; to the sickly and those who, by idiosyncrasy, are strongly affected by the drug.

The methods of using tobacco which the writer considers most harmful will be found below, their harmfulness being in direct ratio with the order here given:—

1st. Chewing.
2d. Cigarette smoking.
3d. Cigar smoking.
4th. Pipe smoking.
5th. Turkish pipe smoking.

The quality of the drug governs the degree of its harmfulness more stringently in some cases than in others, as does also the character and constituents of the paper in which cigarettes are wrapped. This paper is not one in which a discussion of the *impurities* of manufactured tobacco would be proper, and the writer has not, therefore, taken such possibilities of harm into consideration.

In conclusion, let the writer once more call the attention of the reader to the oft-repeated words "excess" and "moderation." These two words, after all, form the keystones of the arches which writers on tobacco, *pro* and *con*, have raised.

PRODUCT, AREA, VALUE, VALUE PER POUND, YIELD PER ACRE, AND VALUE PER ACRE, OF TOBACCO, FOR YEARS 1881, 1882, 1883.

1881.

STATES AND TERRITORIES.	TOTAL PRODUCTION.	TOTAL AREA.	TOTAL VALUE.	AVERAGE VALUE PER POUND.	AVERAGE YIELD PER ACRE.	AVERAGE VALUE PER ACRE.
	Pounds.	*Acres.*	*Dollars.*	*Cents.*	*Pounds.*	*Dols. Cts.*
New Hampshire...	172,551	92	20,706	12	1876	225.12
Vermont.....	132,736	85	19,910	15	1562	234.30
Massachusetts.....	5,000,964	3,291	750,144	15	1520	228.00
Connecticut.....	13,763,759	8,753	2,202,201	16	1572	251.52
New York.....	6,291,217	5,037	880,770	14	1249	174.86
New Jersey.....	181,689	169	21,802	12	1075	129.00
Pennsylvania	38,805,661	33,080	5,044,735	13	1173	152.49
Maryland.....	25,869,218	38,265	2,069,537	8	676	54.08
Virginia.....	77,649,854	139,663	6,677,907	8.6	556	47.82
North Carolina....	24,827,532	56,071	3,351,716	13.5	443	59.80
South Carolina.....	47,528	192	6,653	14	248	34.72
Georgia.....	242,758	1,004	33,986	14	242	33.88
Florida.....	23,085	107	4,617	20	216	43.20
Alabama.....	466,133	2,110	83,903	18	221	39.78
Mississippi	436,000	1,519	74,121	17	287	48.79
Texas.....	217,950	716	39,231	18	304	54.72
Arkansas.....	979,922	2,023	82,313	8.4	484	40.66
Tennessee.....	22,157,300	40,286	1,683,954	7.6	550	41.80
West Virginia.....	2,066,531	4,112	175,655	8.5	503	42.75
Kentucky	163,037,700	232,911	14,347,316	8.8	700	61.60
Ohio.....	35,419,913	36,760	2,833,593	8	964	77.12
Michigan.....	87,706	176	10,963	12.5	498	62.25
Indiana	7,719,373	10,760	578,952	7.5	717	53.77
Illinois.....	3,346,195	5,062	274,387	8.2	661	54.20
Wisconsin.....	8,702,770	10,045	1,087,846	12.5	866	108.25
Missouri.....	12,233,959	13,950	1,015,418	8.3	877	72.79
Other States and Territories.....	.....	...	.....	...	...	...
TOTAL.....	449,880,014	646,239	43,372,336	9.6	696.1	67.11

1882.

STATES AND TERRITORIES.	TOTAL PRODUCTION.	TOTAL AREA.	TOTAL VALUE.	AVERAGE VALUE PER POUND.	AVERAGE YIELD PER ACRE.	AVERAGE VALUE PER ACRE.
	Pounds.	*Acres.*	*Dollars.*	*Cents.*	*Pounds.*	*Dols. Cts.*
New Hampshire..	155,296	110	18,636	12	1412	169.44
Vermont.....	126,099	89	19,393	13	1417	184.21
Massachusetts.....	4,250,819	2,962	531,352	12.5	1435	179.37
Connecticut.....	9,772,269	8,665	1,270,396	13	1128	146.64
New York.....	9,751,386	8,059	1,170,166	12	1210	145.20
New Jersey.....	194,407	172	21,385	11	1130	124.30
Pennsylvania	31,044,529	29,772	3,725,343	12	1043	125.16
Maryland.....	29,232,216	39,030	1,753,933	6	749	44.94
Virginia.....	89,297,332	143,853	6,518,705	7.3	621	45.33
North Carolina....	32,275,792	64,482	3,873,095	12	500	60.00
South Carolina ...	50,380	202	6,549	13	249	32.37
Georgia.....	262,179	1,034	36,705	14	254	35.56
Florida.....	24,239	160	4,363	18	151	27.18
Alabama	475,456	2,173	71,318	15	219	32.85
Mississippi.....	462,171	1,595	60,082	13	290	37.70
Texas	241,924	788	33,869	14	307	42.98
Arkansas.....	1,175,906	2,124	99,952	8.5	554	47.09
Tennessee.....	31,020,220	41,897	2,078,355	6.7	740	49.58
West Virginia.....	2,169,858	4,235	216,986	10	512	51.20
Kentucky.....	198,905,994	242,227	15,912,480	8	821	65.68
Ohio.....	33,648,917	33,819	2,355,424	7	995	69.65
Michigan.....	92,091	181	11,972	13	509	66.17
Indiana	9,108,860	11,298	637,620	7	806	56.42
Illinois.....	3,848,124	5,163	307,850	8	745	59.60
Wisconsin.....	10,443,324	11,250	1,253,199	12	928	111.36
Missouri.....	.....	...	.....	...	...	...
Other States and Territories.....	15,047,770	16,182	1,203,822	8	930	74.40
TOTAL.....	513,077,558	671,522	43,189,951	8.4	764	64.18

1883.

STATES AND TERRITORIES.	TOTAL PRODUCTION.	TOTAL AREA.	TOTAL VALUE.	AVERAGE VALUE PER POUND.	AVERAGE YIELD PER ACRE.	AVERAGE VALUE PER ACRE.
	Pounds.	*Acres.*	*Dollars.*	*Cents.*	*Pounds.*	*Dols. Cts.*
New Hampshire...	145,978	107	18,977	13	1364	177.36
Vermont	.....	...	.....	...	...	...
Massachusetts.....	4,038,278	2,814	533,053	13.2	1435	189.43
Connecticut.....	9,576,824	8,145	1,292,871	13.5	1176	158.73
New York.....	9,068,789	5,440	1,178,943	13	1667	216.72
New Jersey.....	.....	...	.....	...	...	...
Pennsylvania	36,322,099	28,879	4,358,652	12	1258	150.93
Maryland.....	31,570,793	40,593	2,052,102	6.5	778	50.55
Virginia.....	67,865,972	129,996	5,429,278	8	522	41.76
North Carolina....	29,048,213	60,000	3,631,027	12.5	484	60.52
South Carolina....	.....	...	.....	...	...	...
Georgia.....	.....	...	.....	...	...	...
Florida.....	.....	...	.....	...	...	...
Alabama	.....	...	.....	...	...	...
Mississippi.....	.....	...	.....	...	...	...
Texas.....	.....	...	.....	...	...	...
Arkansas.....	1,100,000	2,300	95,700	8.7	478	41.61
Tennessee.....	28,538,602	40,221	1,712,316	6	710	42.57
West Virginia.....	1,952,872	4,108	205,052	10.5	475	49.92
Kentucky.....	171,059,155	230,116	14,711,087	8.6	743	63.93
Ohio.....	29,947,536	32,128	2,395,803	8	932	74.57
Michigan.....	.....	...	.....	...	...	...
Indiana	8,471,240	11,863	635,343	7.5	711	53.56
Illinois.....	3,155,462	5,679	252,437	8	556	44.45
Wisconsin.....	5,743,828	12,750	631,821	11	450	49.55
Missouri.....	10,540,000	15,400	895,900	8.5	684	58.18
Other States and Territories.....	3,400,000	8,200	425,000	12.5	415	51.83
TOTAL.....	451,545,641	638,739	40,455,362	9	707	63.34

Bureau of Statistics of the Department of Agriculture,
Dec. 4th, 1884.

J. R. DODGE,
Statistician.

ESTIMATED AREA, PRODUCT AND VALUE OF THE TOBACCO CROPS, FROM 1868 TO 1883, INCLUSIVE.

Years.	Total Production.	Total Area.	Total Value.	Average Value Per Pound.	Average Yield Per Acre.	Average Value Per Acre.
	Pounds.	*Acres.*		*Cents.*	*Pounds.*	
1868	402,000,000	536,000	$42,612,000	10.6	750	$79.50
1869	393,000,000	604,000	41,265,000	10.5	650.7	68.32
1870	385,000,000	575,000	38,500,000	10	669.6	66.96
1871	426,000,000	580,000	41,748,000	9.8	734.5	71.98
1872	480,000,000	584,600	49,920,000	10.4	821.1	85.39
1873	506,000,000	653,000	41,998,000	8.3	774.9	64.32
1874	315,000,000	500,000	34,650,000	11	630	69.30
1875	522,000,000	710,000	41,760,000	8	735.2	58.82
1876	535,000,000	733,000	39,590,000	7.4	729.9	54 01
1877	580,000,000	745,000	40,600,000	7	778.5	54.50
1878	429,200,000	580,000	32,190,000	7.5	740	55.50
1879	471,000,000	638,841	36,750,000	7.8	737.3	57.53
1880	460,000,000	610,000	39,100,000	8.5	754.1	64.10
1881	450,880,014	646,239	43,372,000	9.6	697.7	67.11
1882	513,077,558	671,522	43,189,951	8.4	764	64.18
1883	451,545,641	638,739	40,455,362	9	707	63.34

Bureau of Statistics, Dep't of Agriculture,
Dec. 4th, 1884.

J. D. DODGE,
Statistician.

A SUMMARY OF THE PHYSIOLOGICAL ACTION.

The conclusions which the writer has reached are as follows:—

1. Tobacco smoking does not decrease the urine eliminated, but rather increases it.

2. Tobacco does retard tissue waste.

3. Tobacco and its alkaloid cause convulsions in the primary stage of the poisoning, by depressing the reflex inhibitory centres in the cord.

4. It causes the palsy of the second stage, by paralyzing (*a*) the motor nerve trunks, (*b*) the motor tract of the spinal cord.

5. That the sensory nerves are not affected by the drug.

6. That Nicotine CONTRACTS the pupil, by stimulating the oculo-motor and paralyzing the sympathetic, this action being peripheral.

7. That Nicotine primarily lowers the blood pressure and pulse rate; (*a*) secondarily, increases pressure and rate; (*b*) thirdly, decreases pressure.

8. That the primary lowering of pressure and rate is due to pneumogastric stimulation, associated with vaso-motor dilatation.

9. That the secondary stage is due to vaso-motor constriction and pneumogastric palsy.

10. That the third stage is due to vaso-motor dilatation returning.

11. That death in poisoning from this drug is due to failure of respiration, the action of the drug being centric.

12. That the blood corpuscles are broken up and crenated by the action of the poison.

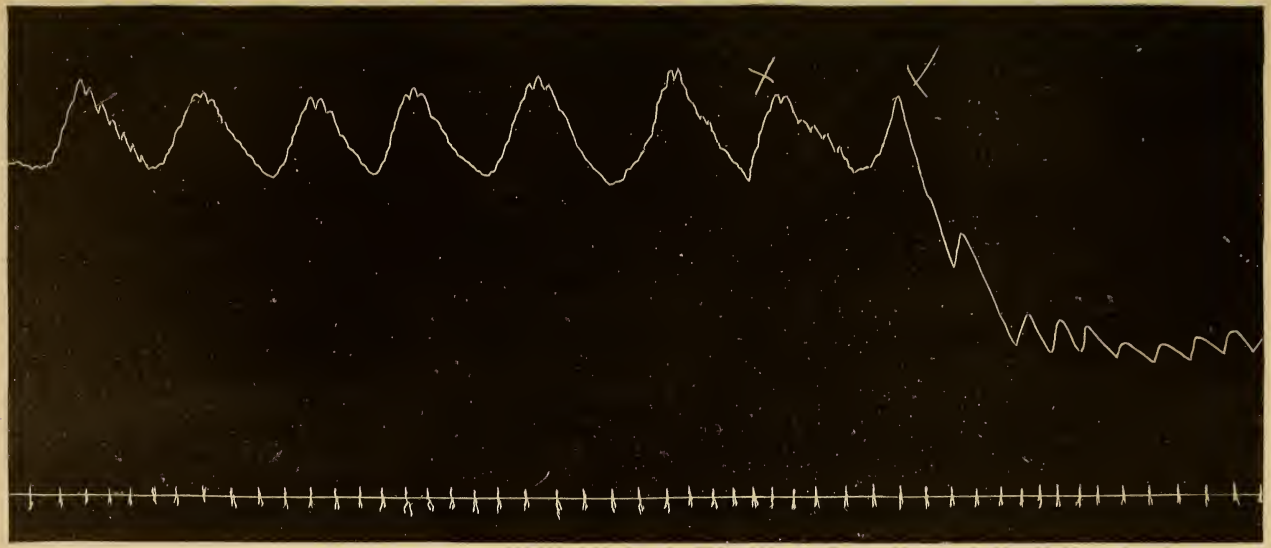
13. That in death from Nicotine poisoning the blood shows changes in *spectra*.

14. That death can be brought about by the cutaneous absorption of Nicotine.

15. That tobacco increases intestinal peristalsis in moderate amounts, and produces tetanoid intestinal spasms in poisonous doses.

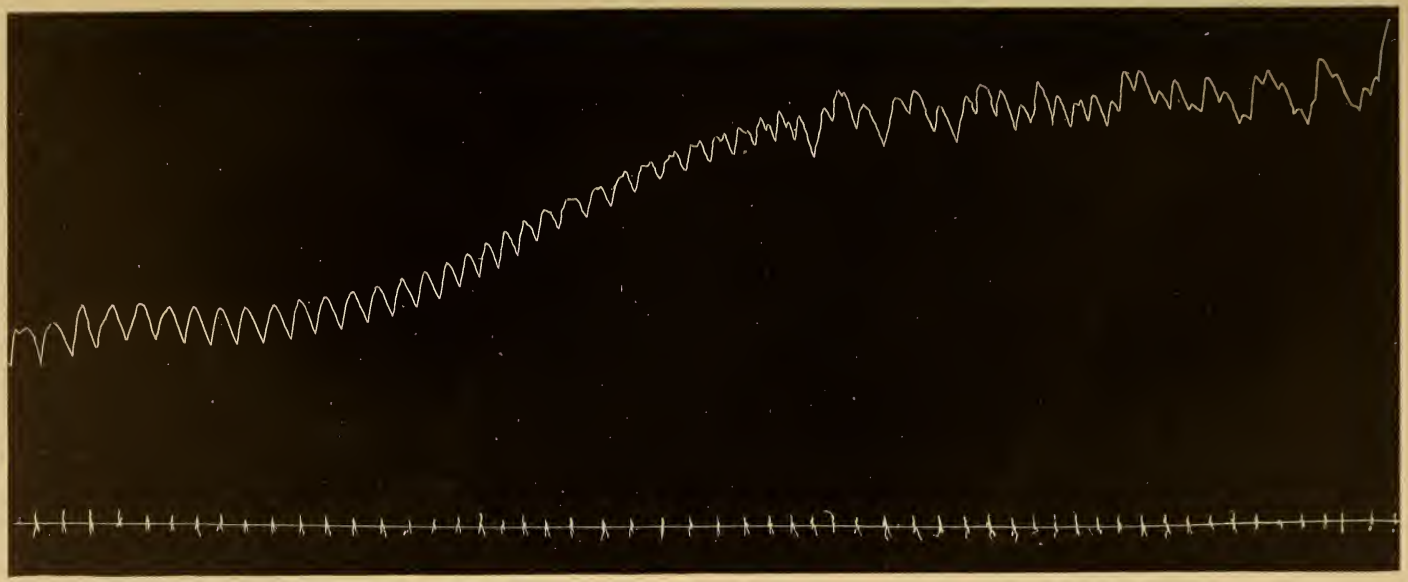
16. That the liver seems to destroy the poison, although this destruction is participated in by any set of capillaries in other parts of the body.

17. That tobacco smoking increases pulse rate and decreases arterial pressure.

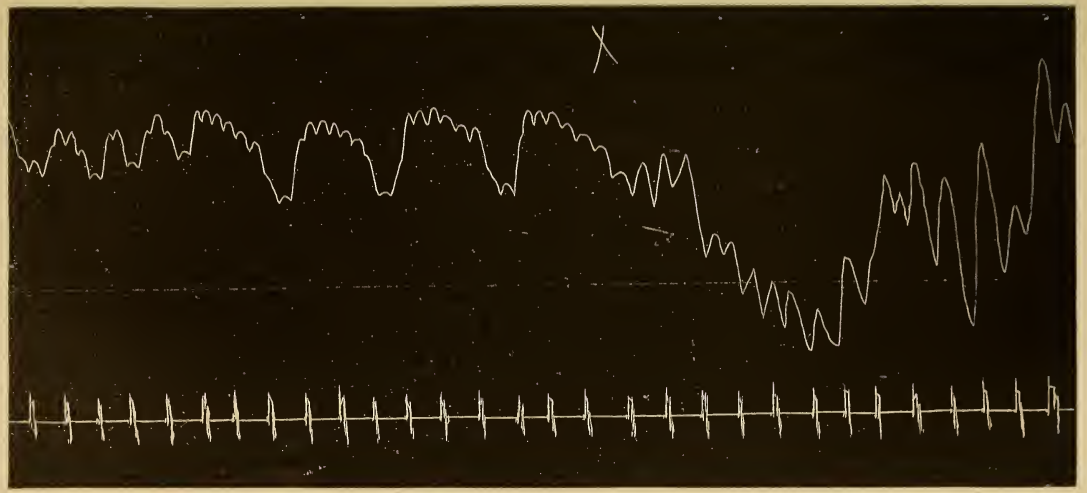


Dog No. 1.—Showing depression (primary) after injection into Jugular vein of $\frac{1}{32}$ drop of Nicotine. + mark shows moment of injection.

Tracing continued on next page.

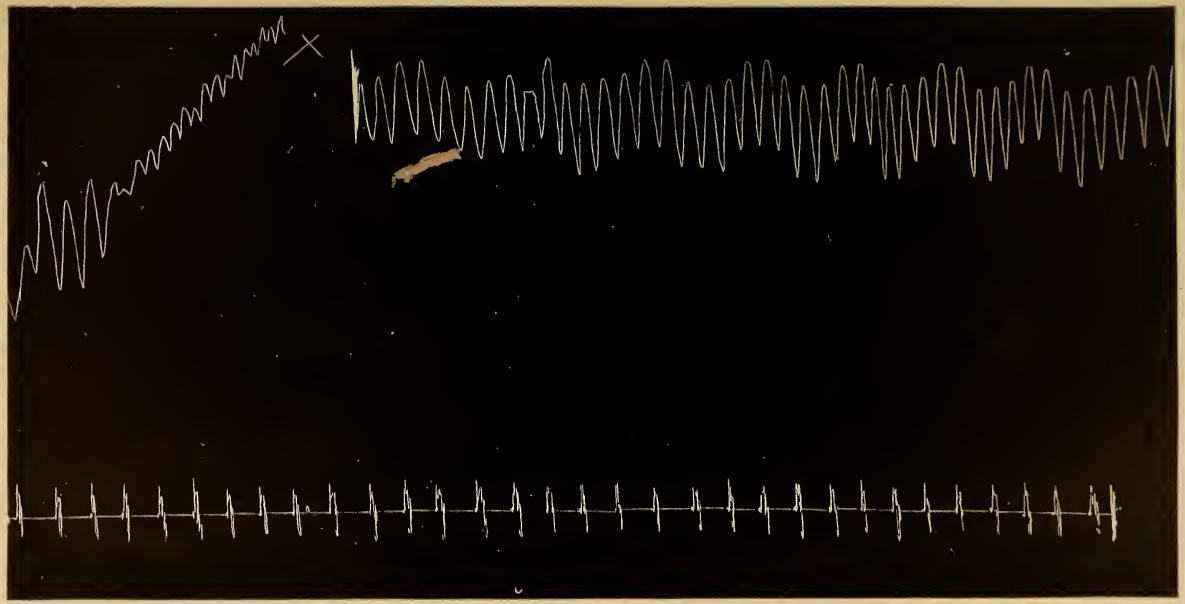


Tracing of Dog No. 1.—*Continued.*—Showing increase of pulse rate and force in second stage, following primary depression. Also, point at which the increased blood pressure sent the pen above the drum.

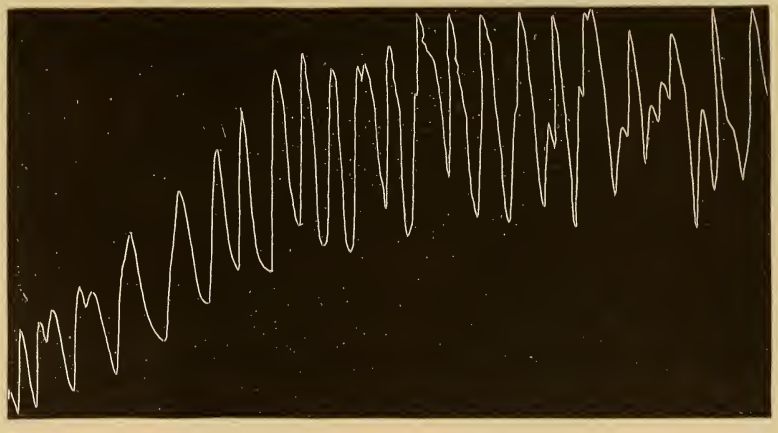


Dog No. 2.—Showing depression from injection into the Jugular vein of $\frac{1}{32}$ drop of Nicotine. Also, showing the rise, first beginning, of second stage. + mark shows point at which injection was made.

Tracing continued on next page.



TRACING OF DOG NO. 2.— *Continued.*—Showing continuation of rise, as seen in first tracing, on last page. Also, showing point at which the blood pressure sent the pen above the drum, and tracing after interval of three minutes after pen went above the drum.



Asphyxia curves produced by a sudden and large injection of Nicotine.

SPHYGMOGRAPHIC TRACINGS OF RADIAL PULSE AFTER TOBACCO SMOKING, AND BEFORE.

All tracings taken in 13 seconds.

TRACINGS TAKEN AFTER SUPPER. NO TOBACCO USED.

= 12, or 60 per minute.

= 12, or 60 per minute.

= 12, or 60 per minute.

= 14, or 70 per minute.

AVERAGE = 12⅛, or 62½ PER MINUTE.

SPHYGMOGRAPHIC TRACINGS OF RADIAL PULSE AFTER TOBACCO SMOKING, AND BEFORE.—*Continued.*

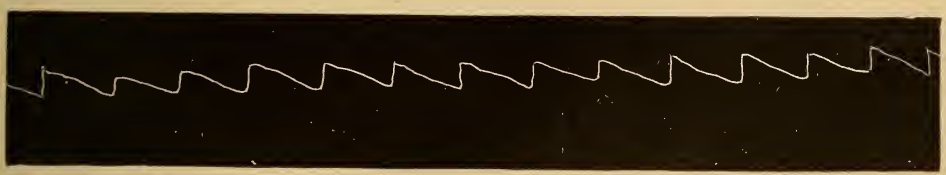
All tracings taken in 13 seconds.

TRACINGS TAKEN AFTER SUPPER. TOBACCO USED, ONE CIGARETTE.

= 14, or 70 per minute.

= 15, or 75 per minute.

= 14, or 70 per minute.



= 14, or 70 per minute.

AVERAGE = 14¼, or 71¼ PER MINUTE.

Average, with tobacco,	71¼	per minute.
" without tobacco,	62½	" "
Increase,	8¾	per minute.

FISKE FUND PRIZE DISSERTATION, No. XXXIV.

THE PHYSIOLOGICAL AND PATHOLOGICAL EFFECTS OF THE USE OF TOBACCO.

BY

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